HCV Viral Load

See Technical Bulletin- Reporting Change HCV Real Time PCR Viral Load

With the incorporation of the *COBAS® AmpliPrep/COBAS® TaqMan® HCV Test, v2.0* (Roche Diagnostics) the HCV Viral Load reportable range is now 15 IU/mL to 100,000,000 IU/mL.

HCV viral load monitoring plays a significant role in the management of patients under these therapies.

- Quantitative results will be reported for HCV viral loads ranging from 15 IU/mL to 100,000,000 IU/mL (1.18 Log_{10} IU/mL to 8.0 Log_{10} IU/mL).
- Results reported as <15 IU/mL (<1.18 Log_{10} IU/mL) should be interpreted as **Detected**, but below the limit of quantification.
- Results reported as **Not Detected** are below the limit of detection.
- The test provides clinical results which correlate closely to the *COBAS® AmpliPrep/COBASTaqMan HCV Test*, with an average Log difference in patient samples of ~0.1 Log IU/mL. This same level of result correlation is evident around the lower limit of quantitation of 15 IU/mL. Further, the test produces similar results to the Roche real-time PCR test utilized in two clinical trials which supported the approval of currently available direct-acting antivirals (the *COBAS® TaqMan® HCV Test v2.0 for use with High Pure System*), demonstrating an average Log difference in patient samples of 0.1 Log IU/mL. Based on these analytical performance characteristics and the high degree of correlation between testing methodologies, it is unlikely that a significant difference in detectable virema will be observed when comparing identical patient samples.

Hepatitis C virus is considered to be the principal etiologic agent responsible for 90% to 95% of cases of post transfusion hepatitis. HCV is a single stranded positive sense RNA virus with a genome of approximately 9,500 nucleotides coding for 3,000 amino acids. As a blood borne virus, HCV is transmitted by blood and blood products. Widespread adoption of HCV blood screening measures has markedly lowered the risk of transfusion associated hepatitis. The incidence of HCV infection is the highest in association with intravenous drug abuse and to a lesser extent with other percutaneous exposures. The global prevalence of HCV infection is estimated to be 3% and the prevalence in the USA was 1.6% between 1999 and 2003. Following exposure, 75% to 85% of HCV infected individuals develop chronic hepatitis, with up to 20% of these chronic cases progressing to cirrhosis. In cirrhotic patients, hepatocellular carcinoma is observed in 1% to 4% of the population every year.

Quantitation of HCV RNA for measuring baseline viral loads and for on-treatment monitoring has been well established in demonstrating the efficacy of antiviral response to pegylated interferon plus ribavirin combination therapy. Current guidelines for the management and treatment of HCV recommended quantitative testing for HCV RNA before the start of antiviral therapy, during therapy (response guided therapy), and generally 12 to 24 weeks following the end of treatment. Absence of detectable HCV RNA by a sensitive test, 24 weeks after the end of treatment, is the goal of treatment and indicates that a sustained virologic response (SVR) has

been achieved. During antiviral therapy, an early virologic response (EVR) defined as a two log or greater decrease in HCV RNA, or undetectable HCV RNA after 12 weeks of therapy, is commonly observed. Failure to achieve an EVR has a high negative predictive value for achieving a SVR and has been incorporated in the futility (stopping) rules for pegylated interferon plus ribavirin therapies. A rapid viral response (RVR), undetectable levels of HCV RNA after 4 weeks of therapy, has a high positive predictive value for SVR.

HCV RNA can be detected in plasma using nucleic acid extraction and amplification technologies. The *COBAS® AmpliPrep/COBAS® TaqMan® HCV Test, v2.0* uses real time PCR technology combined with a novel dual probe approach for the accurate quantitation of HCV RNA. Novel primers allow for the detection and quantitation of genotypes 1,2,3,4,5 and 6. The assay is standardized against the WHO International Standard for Hepatitis C Virus RNA for Nucleic Amplification Technology Assays and titer results are reported in International Units per milliliter (IU/mL).

Notes:

Quantitation of HCV RNA is dependant on the number of virus particles present in the specimen and may be affected by specimen collection methods, patient factors (e.g. age, presence of symptoms) and stage of infection.

The *COBAS® AmpliPrep/COBAS® TaqMan® HCV Test, v2.0* is not intended for use as a screening test for the presence of HCV in blood or blood products or as a diagnostic test to confirm the presence of HCV infection.

Though rare, mutations in the highly conserved regions of the viral genome covered by the *COBAS® AmpliPrep/COBAS® TaqMan® HCV Test v2.0* primers and/or probe may result in the under-quantitation of or failure to detect the presence of the virus in this circumstance.

Results will be reported as HCV RNA IU/mL and Log_{10} IU/mL.

References

VICTRELIS™ (boceprevir) prescribing information issued 9/2013

INCIVIK™ (telaprevir) prescribing information issued in 4/2013

Cobas® AmpliPrep/Cobas® TaqMan® HCV Test, v2.0 package insert, 03/2013, Doc Rev 1.0

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