We see what truly matters

HCV viral load testing
HCV - an ever changing virus
Sequence diversity challenges viral load tests

Hepatitis C virus (HCV) is a major cause of progressive liver disease. About 150 million people are infected with HCV, 80% of them chronically, and more than 350,000 people die every year from HCV induced complications like liver cirrhosis and carcinoma.\textsuperscript{1,2} This calls for worldwide efforts to improve diagnosis and treatment of chronic hepatitis C.

HCV is characterized by a high replication rate combined with a high mutation rate resulting in an extreme genetic variability. Over time HCV has evolved into 6 genotypes and more than 50 subtypes, but even within the infected patient HCV is continuously developing into new sequence variants.\textsuperscript{3,4,5}

This large and dynamic sequence heterogeneity of the HCV genome continues to challenge HCV viral load tests as it can lead to mismatches in their target region.\textsuperscript{6,7} Scientist developing such tests have thus to introduce special measures to ensure accurate detection and quantitation of HCV across variants.
Technology advances for better reliability

Two probes are better than one

Accurate HCV viral load monitoring is essential for current and future HCV treatments: to evaluate virological response, guide treatment duration, and decide on futility. This demands an HCV RNA assay that can correctly distinguish true signals from background noise. Roche’s new HCV viral load assay provide improvements such as:

- Two non-overlapping detection probes in combination with two staggered downstream primers to ensure reliable assay performance with a wide range of HCV isolates and high sequence heterogeneity.

- Improved mismatch tolerance enabling the test to accurately quantify the target despite nucleotide changes in the viral genome while maintaining high specificity for HCV RNA.

- A new blend of DNA polymerases in combination with an optimized PCR protocol enhances fidelity and efficiency.

These key design changes result in a robust quantitative test that meets the requirements for HCV RNA testing in the new era of DAA therapy.
Given the genetic variability of HCV and the selective pressures contributed by DAAs, it is important for a test to be designed to tolerate mismatches to ensure accurate quantitation of the target.

Mismatch tolerance has to be carefully balanced with specificity requirements. Too much mismatch tolerance (like applying low stringency probe binding conditions\(^{14,15,16}\)) can potentially cause detection of non-HCV sequences resulting in falsely high values. This may eventually lead to suboptimal patient management.

The latest quantitative HCV assay from Roche Molecular Diagnostics is based on a novel dual probe approach with an optimized automated extraction and amplification procedure. This ensures highly sensitive detection of HCV RNA across different HCV genotypes with accurate and reproducible results at low viral loads.
**Technological advances for better reliability.**

The novel dual-probe assay design for the COBAS® AmpliPrep/COBAS® TaqMan® HCV Test, v2.0 provides built-in redundancy and improved mismatch tolerance for confidence in viral load monitoring.

- Addition of a second probe in the 5' NTR region of the HCV genome as well as an additional reverse primer.

- Helps to safeguard against PCR inefficiencies and potential polymorphisms that may occur in the genome of constantly evolving virus.

- Long term strategy against mutations that may occur with current or future therapies.
Better diagnostics for better patient management

The COBAS® AmpliPrep/COBAS® TaqMan® HCV Test, v2.0

The goal to improve therapy management of chronically HCV infected patients calls for a joint effort between researchers, diagnostic laboratories and clinicians.

The innovative, state-of-the-art dual-probe HCV viral load assay from Roche Molecular Diagnostics precisely distinguishes true signals from background noise leading to more accurate quantification of viral load.17

Accurate HCV RNA viral load results are particularly important for monitoring patients treated with DAAs to assess eligibility for shortened treatment or the need to invoke the futility rules during RGT.

The Roche dual-probe HCV viral load assay helps clinicians to better manage HCV patients facilitating optimized clinical decisions and contributing to our collective goal of stopping the spread of HCV.

Together, we can set a new standard.
References

2. WHO Hepatitis C Fact sheet N°164, July 2013 (http://www.who.int/mediacentre/factsheets/fs164/en/)
17. Pfeifer HK and Sarrazin C. The importance of HCV RNA measurement for tailoring treatment duration. Digestive and Liver Disease, 2013; 45S: 323–331