Hepatitis Viruses

Hepatitis Viruses are a group of infectious liver diseases caused by hepatotropic viruses belonging to different families. There are 5 major viruses that cause hepatitis. They make up two groups of hepatitis: enteric (HAV and HEV) and parenteral (HBV, HCV and HDV).

	HEPATITIS A	HEPATITIS B	HEPATITIS C	HEPATITIS D	HEPATITIS E
AGENT	Hepatitis A virus (HAV);single stranded RNA; no envelope	Hepatitis B virus (HBV);double stranded DNA; envelope	Hepatitis C virus (HCV); single stranded RNA; envelope	Hepatitis D virus (HDV); single stranded RNA; envelope from HBV	Hepatitis E virus (HEV); single stranded RNA; no envelope
FAMILY	Picornaviridae	Hepadnaviridae	Flaviviridae	Deltavirus (viroid)	Calicivirus
GENOME	RNA: 7500 nc	DNA: 3200 nc	RNA: 9500 nc	RNA: 1700 nc	RNA: 7500 nc
TRASMISSION WAY	Fecal-Oral	Parenteral	Parenteral	Parenteral	Fecal-Oral
CHRONIZATION	No	Yes	Yes	Yes	No
INCUBATION TIME	15-50 days	45-160 days	14-180 days	Uncertain	15-50 days
MANIFESTATION OR SYMPTOMS	Mostly subclinical; severe cases: fever, headache, malaise, jaundice	Mostly subclinical; similar to HAV, but fever, headache absent, and often progress to severe liver damage	Similar to HBV	Severe liver damage, high mortality rate	Similar to HAV, but pregnant women may have high mortality rate
VACCINES	Yes	Yes	None	HBV vaccine is protective because coinfection required	None

Hepatitis A (HAV)

The ***hepatitis A (HAV)*** virus is the enteric infection most widely spread in the world. This is the acute infectious disease of liver transmitted by fecal-oral way, the causative agent of which is hepatitis A virus (HAV) belonging to the family Picornaviridae. Virus hepatitis A is one of the five most economically significant infectious diseases and one of the priority problems of the public healthcare.
Detection of the causative agent RNA by PCR method has significant advantages as related to ELISA and biochemical tests at detection of the virus in blood of contact persons as RNA of the hepatitis A virus manifests itself in the blood on the third week from the moment of contamination and is detected at the average within 20 days after appearance of the disease symptoms. Thus, RNA is the first diagnostic marker detected in the patient blood, occurs earlier than HAV IgM and gives no false negative reactions.

Hepatitis A Virus Kits

TV4-50FRT SA, RG, iQ, SC,MX, A,B,LC	**HAV Real-TM Qual** Complete Real Time Test with Ribo-Sorb extraction kit	**R**	CE	50	5 x10^2 copies/ml
TV4-50FRT C SA, RG, iQ, SC,MX, A,B,LC	**HAV Real-TM Qual** Complete Real Time Test with Ribo-Virus column extraction kit	**R**	CE	50	5 x10^2 copies/ml
V4-50FRT SA, RG, iQ, SC,MX, A,B,LC	**HAV Real-TM Qual** Real Time Amplification kit with the RNA extraction controls	**R**	CE	50	5 x10^2 copies/ml

Hepatitis B (HBV)

Hepatitis B virus (HBV) is a widely spread human infection caused by DNA-containing virus of hepatitis B belonging to the family Hepadnaviridae. Transmission of hepatitis B virus results from exposure to infectious blood or body fluids containing blood. Possible forms of transmission include unprotected sexual contact, blood transfusions, re-use of contaminated needles & syringes, and vertical transmission from mother to child during childbirth. The viral hepatitis B presents a serious problem for public healthcare due to its universal spread. At present in accordance with the WHO data the population infected with hepatitis B virus makes 500 million people.

Detection of HBV DNA is used for:

- Early diagnostics of acute viral hepatitis B;
- Detection of latent forms of viral hepatitis B;
- Detection of mutant strains of hepatitis B virus by HBsAg;
- Establishment of diagnosis of chronic viral hepatitis B;
- Monitoring of effectiveness of the antiviral therapy;

ADVANTAGES OF SACACE™ HBV REAL-TM QUANT DX CE-IVD MARKED KIT

Key Features

- Primers and probes in highly conserved 5'-gene (coding the surface antigen of the hepatitis B virus HBsAg) region of the HBV genome.
- **Reagents lyophilized** and aliquoted
- Excellent **sensitivity** of **7 IU/ml** (1 ml input)
- Relults expressed directly in International Units
- Use of exogenous **internal control** to check extraction and amplification
- 1 Low and 1 High concentrated extraction positive controls, to be extracted as the samples
- Reagents can be **stored at 4°C** and **shipped at room temperature**
- Very **long shelf life** (1 year)

Advantages

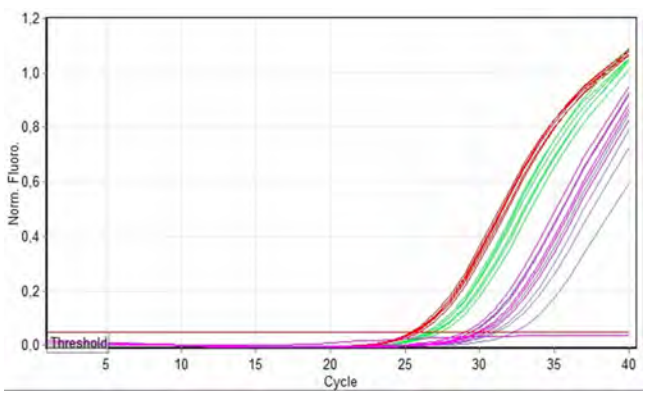
- No need of PCR mix setup
- No possibility of mistake during reagent dispensing
- No problem with storage
- No need for refrigerated transportation
- No possibility of reagent components contamination

Very Easy To Use

No more need to prepare PCR mastermix! The HBV Real-TM Quant DX kit contains **96 ready to use 0.2 ml PCR tubes where you just need to add your extracted viral DNA. That's it!**

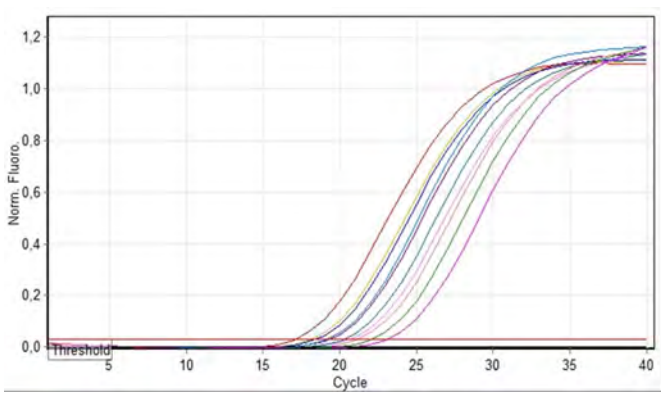
The reaction tubes are ready to be transfereed into the Real Time PCR thermal cycler.

Excellent sensitivity (LOD)



The Limit Of Detection of 7 IU/ml was determined by testing dilutions of the 3rd WHO International Standard for Hepatitis B Virus for Nucleic Acid Amplification Tecniques (NIBSC code: 10/264) prepared in HBV negative human plasma. The results were determined by Probit analysis.

Optimal specificity



Most relevant HBV genotypes (A-B-C-D-H) were tested analyzing dilution series and results showed good and clear sigmoid-shaped fluorescence curves and a Cycle threshold (Ct) less than 35.

Hepatitis B Virus Kits

V5-96/3FRT SA, RG*	**HBV Real-TM Quant DX** Real Time Amplification kit with positive controls and standards, 96 ready to use lyophilized PCR tubes * validated on SA and RG, but optimized also on iQ,SC,MX,A,B	**R**	CE	96	Linearity: 7 - 10^8 IU/ml
TV5-100/2FRT SA, RG, iQ, SC,MX, A,B	**HBV Real-TM Quant** Complete Real Time Test with Ribo-Sorb extraction kit (25 µl Reaction Mix)	**R**		100	Linearity: 3 x10^2 -10^8 copies/mL
TV5-100/2FRT C SA, RG, iQ, SC,MX, A,B	**HBV Real-TM Quant** Complete Real Time Test with Ribo-Virus column extraction kit (25 µl Reaction Mix)	**R**		100	Linearity: 2 x10^2 -10^8 copies/mL
V5-100/2FRT SA, RG, iQ, SC,MX, A,B	**HBV Real-TM Quant** Real Time Amplification kit with the DNA extraction controls (25 µl Reaction Mix)	**R**		100	Linearity: 50 -10^8 copies/mL
TV5-100FRT SA, RG, iQ, SC,MX, A,B,LC	**HBV Real-TM Qual** Complete Real Time Test with Ribo-Sorb extraction kit (25 µl Reaction Mix)	**R**		100	2 x10^2 copies/ml
TV5-100FRT C SA, RG, iQ, SC,MX, A,B,LC	**HBV Real-TM Qual** Complete Real Time Test with Ribo-Virus column extraction kit (25 µl Reaction Mix)	**R**		100	1 x10^2 copies/ml
V5-100FRT SA, RG, iQ, SC,MX, A,B,LC	**HBV Real-TM Qual** Real Time Amplification kit with the DNA extraction controls (25 µl Reaction Mix)	**R**		100	50 copies/ml
TV5-64FRT SA, RG, iQ, SC,MX, A,B,LC	**HBV Real-TM Qual** Complete Real Time Test with Ribo-Sorb extraction kit (50 µl Reaction Mix)	**R**		64	1 x10^2 copies/ml

Hepatitis B Genotyping

Hepatitis B virus (HBV) infects nearly two billion people worldwide. The hepatitis B virus (HBV) is currently categorized into eight genotypes (A to H). Genotypes have been found to be geographically distributed. Numerous studies have investigated the clinical implications of HBV genotypes to disease severity, response to IFN, disease chronicity and hepatocellular carcinoma (HCC).

Hepatitis B Genotyping Kits

R5-Gen SA, RG, iQ, SC,MX, A,B	**HBV Genotype A, B, C, D Real-TM** Real Time Amplification kit	**R**	50

Hepatitis C (HCV)

Hepatitis C virus (HCV) is RNA-containing, hepatotropic virus belonging to the Flaviviridae family. Contamination with hepatitis C virus occurs at direct entering of the virus in blood (at parenteral interventions or during blood transfusions). Most people with acute HCV infection are asymptomatic or have mild symptoms (fatigue, nausea, jaundice) but they are unable to clear the virus and in approximately 80% of cases this leads to chronic infection. In 15 to 20% of patients chronic HCV infection progresses at a variable rate to cirrhosis, with a 1 to 4% annual risk of developing hepatocellular carcinoma.

ADVANTAGES OF SACACE™ HCV REAL-TM QUANT DX CE-IVD MARKED KIT

Key Features

- Primers and probes in highly conserved 5' UTR region of the HCV genome
- **Reagents lyophilized** and aliquoted
- Excellent **sensitivity** of **13 IU/ml** (1 ml input)
- Relults expressed directly in International Units
- Use of exogenous **internal control** (RNA) to check extraction and amplification
- 1 Low and 1 High concentrated extraction positive controls, to be extracted as the samples
- Reagents can be **stored at 4°C** and **shipped at room temperature**
- Very **long shelf life** (1 year)

Advantages

- No need of PCR mix setup
- No possibility of mistake during reagent dispensing
- No problem with storage
- No need for refrigerated transportation
- No possibility of reagent components contamination

Very Easy To Use

No more need to prepare PCR mastermix! The HCV Real-TM Quant DX kit contains **96 ready to use 0.2 ml PCR tubes where you just need to add your extracted viral RNA. That's it!**
The reaction tubes are ready to be transfereed into the Real Time PCR thermal cycler.

ITC

Notified Body 1023
INSTITUTE FOR TESTING AND CERTIFICATION, Inc.,
třída Tomáše Bati 299, Louky, 763 02 Zlín, Czech Republic

EC Certificate - Full Quality Assurance System
No. 13 0673 QS/NB

The quality system of manufacturer

Sacace Biotechnologies S.r.l.
via Scalabrini, 44, 22100 Como, Italy

has been certified as meeting the requirements of

Directive 98/79/EC
on in vitro diagnostic medical devices, Annex IV excluding (4, 6)

for the following product category(ies):

In Vitro Diagnostic PCR Kits

The Notified Body No. 1023 declares that the aforementioned manufacturer has implemented a quality assurance system for design, manufacture and final inspection of the respective devices / device categories in accordance with IVDD Annex IV. This quality assurance system conforms to the requirements of this Directive and is subjected to periodical surveillance. For placing on the market of List A devices covered by this certificate, an EC Design-Examination Certificate according to Annex IV (Section 4) is required.

Valid from: 2016-09-26
Valid until: 2021-09-25
First Issued: 2013-07-30
Revision: a

Date: 2016-09-26

RNDr. Radomír Čevelík
Representative of the Notified Body No. 1023

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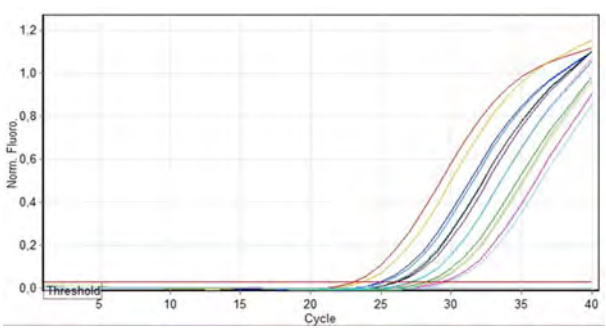
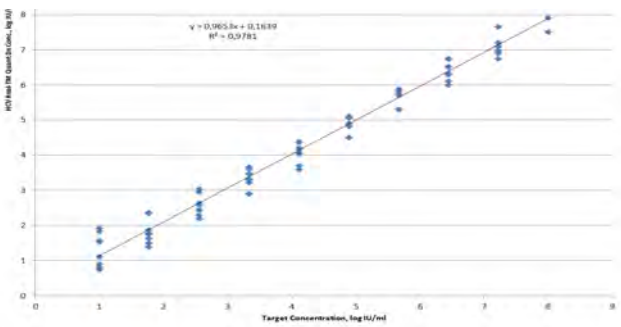
Optimal specificity



Most relevant HCV genotypes (1-2-3-4-5) were tested analyzing dilution series and results showed good and clear sigmoid-shaped fluorescence curves and a Cycle threshold (Ct) less than 35.

Wide linear range



The linear range of the HCV Real-TM Quant DXkit has been determined by analyzing a dilution series (8,00 log IU/ml to 1,00 log IU/ml) of an HCV synthetic quantitative standard calibrated against the 4th WHO International HCV RNA Standard.

Hepatitis C Virus Kits

V1-96/3FRT SA, RG*	**HCV Real-TM Quant DX** Real Time Amplification kit with positive controls and standards, 96 ready to use lyophilized PCR tubes * validated on SA and RG, but optimized also on iQ,SC,MX,A,B	**R**	CE	96	Linearity: 13 - 10^8 IU/ml
TV1-100/2FRT SA, RG, iQ, SC,MX, A,B,	**HCV Real-TM Quant** Complete Real Time Test with Ribo-Sorb extraction kit (25 µl Reaction Mix)	**R**		100	Linearity: 3 x10^2 - 5 x10^7 IU/mL
V1-100/2FRT SA, RG, iQ, SC,MX, A,B	**HCV Real-TM Quant** Real Time PCR kit with the RNA extraction controls (25 µl Reaction Mix)	**R**		100	Linearity: 50 - 5 x10^7 IU/mL
TV1-100/2FRT C SA, RG, iQ, SC,MX, A,B	**HCV Real-TM Quant** Real Time PCR kit with Ribo-Virus column extraction kit (25 µl Reaction Mix)	**R**		100	Linearity: 2 x10^2 - 5 x10^7 IU/mL
TV1-100FRT SA, RG, iQ, SC,MX, A,B,LC	**HCV Real-TM Qual** Complete Real Time Test with Ribo-Sorb extraction kit (25 µl Reaction Mix)	**R**		100	2 x10^2 IU/mL
TV1-100FRT C SA, RG, iQ, SC,MX, A,B,LC	**HCV Real-TM Qual** Complete Real Time Test with Ribo-Virus column kit (25 µl Reaction Mix)	**R**		100	1 x10^2 IU/mL
V1-100FRT SA, RG, iQ, SC,MX, A,B,LC	**HCV Real-TM Qual** Real Time PCR kit with the RNA extraction controls (25 µl Reaction Mix)	**R**		100	50 IU/mL

HCV associated infection kits

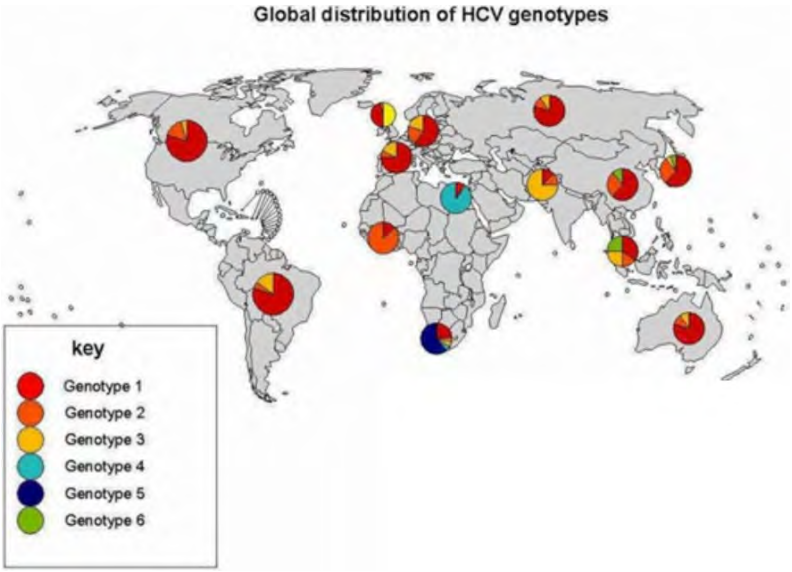
Interleukin-28 (IL28) is a cytokine that plays a role in immune defense against viruses. IL28B belongs to the type III interferon family of cytokines. Its classification as interferon is due to its ability to induce an antiviral state. Polymorphisms in the IL28B gene region are important in predicting outcome following therapy for chronic hepatitis C virus (HCV) infection.
Combined therapy IFN pegylated (PEG-IFN) and ribavirin (RBV) is the current standard therapy against HCV infection and to know in detail the polymorphism in IL28B gene region of patients infected with HCV can be an important component of the decision to initiate treatment with PEG-IFN and RBV.

HCV associated infection kits

R05-100FRT SA, RG, iQ, MX, A, B	**IL28B rs17 / rs60 Real-TM** Real Time amplification kit	**R**	CE	100	

Hepatitis C Virus Genotyping

HCV is classified into eleven major genotypes (designated 1-11), many subtypes (designated a, b, c, etc.), and about 100 different strains (numbered 1,2,3, etc.) based on the genomic sequence heterogeneity. Genotypes 1-3 have a worldwide distribution. Types 1a and 1b are the most common, accounting for about 60% of global infections. They predominate in Northern Europe and North America, and in Southern and Eastern Europe and Japan, respectively. Type 2 is less frequently represented than type 1. Type 3 is endemic in south-east Asia and is variably distributed in different countries. Genotype 4 is principally found in the Middle East, Egypt, and central Africa. The determination of the infecting genotype is important for the prediction of response to antiviral treatment: genotype 1 and 4 are generally associated with a poor response to interferon alone, whereas genotypes 2 and 3 are associated with more favourable responses. At patients with subtype 1b the disease progresses to a chronic condition 90 % of cases, in that time as with genotypes 2 and 3b in 33-50 %. In a number of works it is mentioned, that infection with 1b genotype have heavier current of disease with development of a cirrhosis and hepatocarcinoma.
The International Consensus European Association for the Study of the Liver (EASL) recommends before beginning of antiviral therapies to carry out a liver biopsies and to determine HCV genotype.



Hepatitis C Virus Genotyping Kits

R1-Gen-4X SA, RG, iQ, MX, SC, A, B	**HCV 1/2/3 Genotype Real-TM** Real Time PCR kit with the RNA extraction controls	**R**	48	1 x10^2 IU/mL
R1-Gen-6 SA, RG, iQ, SC,MX, A, B	**HCV Genotype Plus (1a,1b, 2, 3a, 4, 5a, 6) Real-TM** Real Time PCR kit with the RNA extraction controls	**R**	48	1 x10^2 IU/mL

Hepatitis D (HDV)

Hepatitis D virus (HDV) is RNA containing, hepatotropic viroid (uncompleted virus) belonging to Deltavirus family. HDV needs helper function of hepatitis B virus that provides to HDV proteins of the superficial membrane (HBsAg) that's why HDV can replicate itself only in presence of HBV. Transmission of HDV can occur either via simultaneous infection with HBV (coinfection) or via infection of an individual previously infected with HBV (superinfection). Both superinfection and coinfection with HDV results in more severe complications compared to infection with HBV alone. These complications include a greater likelihood of experiencing liver failure in acute infections and a rapid progression to liver cirrhosis, with an increased chance of developing liver cancer in chronic infections. In combination with hepatitis B virus, hepatitis D has the highest mortality rate of all the hepatitis infections of 20%.
Detection of HDV RNA by PCR allows detection of the causative agent in the period of introduction of infection before seroconversion, which is very important for early diagnostics.

Hepatitis D Virus Kits

V3-100FRT SA, RG, iQ, SC,MX, A,B,LC	**HDV Real-TM Qual** Real Time PCR kit with the DNA extraction controls	**R**	100	1 x10^2 copies/mL
V3-100/2FRT SA, RG, iQ, SC,MX, A, B	**HDV Real-TM Quant** Real Time PCR kit with the DNA extraction controls	**R**	100	1 x10^2 copies/mL
TV56-100FRT SA, RG, iQ, SC,MX, A,B	**HBV/HDV Real-TM** Complete Real Time Test with Ribo-Sorb extraction kit	**R**	100	2 x10^2 /5-10^2 copies/mL
TV56-100FRT C SA, RG,iQ,SC,MX, A,B	**HBV/HDV Real-TM** Complete Real Time Test with Ribo-Virus column kit	**R**	100	1 x10^2 /3-10^2 copies/mL
V56-100FRT SA, RG, iQ, SC,MX, A,B	**HBV/HDV Real-TM** Real Time PCR kit with the DNA/RNA extraction controls	**R**	100	20/100 copies/mL

Hepatitis G (HGV)

Hepatitis G virus (HGV) is another virus causing post-transfusion hepatitis. The same as hepatitis C virus, hepatitis G virus belongs to the flaviviruses. The hepatitis G virus is detected with the help of PCR (serological methods are less reliable). It's detected in 1.5 percent of donors and in some patients with acute fulminant and chronic hepatitis. The coinfection of hepatitis G with hepatitises B, C or D is detected frequently.

Hepatitis G Virus Kits

TV2-50FRT SA, RG, iQ, SC,MX, A,B,LC	**HGV Real-TM** Real Time PCR kit with Ribo-Sorb extraction kit	**R**	50	5 x10^2 copies/mL
V2-50FRT SA, RG, iQ, SC,MX, A,B,LC	**HGV Real-TM** Real Time PCR kit with the DNA extraction controls	**R**	50	3 x10^2 copies/mL