

# Hepatitis E Virus Markers ELISAs

## *What is Hepatitis E virus?*

While HEV infections, endemic and frequently epidemic occur mainly in developing countries, it has also been observed in developed countries sporadically with or without a history of traveling to endemic area. Hepatitis E virus (HEV) is a non-enveloped, single-stranded RNA virus identified in 1990. There are four major genotypes of HEV, but there is only a single serotype. HEV is transmitted primarily through the fecal-oral route, transfusion and possibly maternal-fetal. Infection with HEV induces acute or sub-clinical liver diseases similar to Hepatitis A. However, recent studies revealed that persistent HEV infections do occur, especially in immune-suppressed cases, e.g. organ transplant recipients or HIV infected persons.

The overall case-fatality is 0.5~3%, and it is much higher (15~25%) among pregnant women. Recently, it is reported that Hepatitis E cases with chronic liver disease reached a mortality rate of greater than 70%. A hypothesis that HEV infection is a zoonosis was presented in 1995. Subsequently, a swine HEV and later an avian HEV were identified and sequenced separately in 1997 and 2001, respectively. Since then, HEV infection include anti-HEV, viremia and feces excretion of HEV was observed in a wide variety of animals, i.e., swine, rodents, wild monkeys, deer, cow, goats, dogs, rodents and chicken in both developing and developed countries.



## *Ordering Info*

Cat.	Product	Detection	Specimen	Pack size
WE-7296	HEV-IgG ELISA	Antibody	Serum/Plasma	96T/kit
WE-7196	HEV-IgM ELISA	Antibody	Serum/Plasma	96T/kit
WE-7596	HEV-Ag ELISA <sup>Plus</sup>	Antigen	Serum/Plasma	96T/kit

In developed regions, hepatitis E was previously thought to be rare and restricted to travelers to endemic countries. Data published throughout the last ten years clearly show that locally-acquired hepatitis E in Europe and other developed countries is common. In addition, chronic HEV infection occurs in the immunosuppressed individuals.

**Prevalence rates among different population groups in Europe established with Wantai HEV IgG against other commercially available HEV IgG tests.**

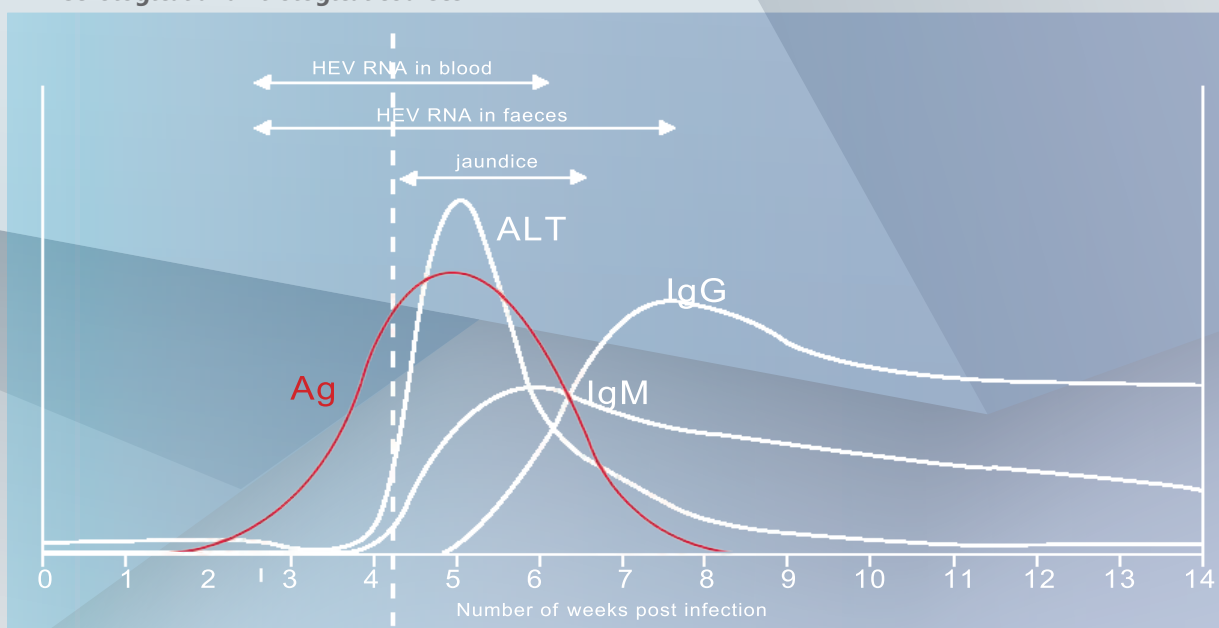
Study cohort	Wantai	Mikrogen	MP	Abbott	Adaltis	Dia.Pro	Others
General Population (%)	16.90	10.11	6.50	2.29	8.72	4.35	12.48
Sample Size (n)	88,204	1777	14,385	1077	nd*	5,176	3667
Liver Disease (%)	16.05	9.55	6.13	2.02	8.2	3.94	11.86
Sample Size (n)	nd*	41	801	129	nd*	nd*	2000
Transplant Recipients (%)	18.36	11.42	7.69	2.97	9.96	5.22	13.91
Sample Size (n)	415	124	1328	262	64	448	52
HIV (%)	15.69	9.26	5.90	1.88	7.93	3.75	11.55
Sample Size (n)	2047	nd*	1579	123	429	548	238
Swine/ Animal Contact (%)	28.51	20.13	15.26	8.37	18.25	11.82	23.21
Sample size (n)	101	709	1354	202	43	nd*	995

**Calculated seroprevalence rates for the general population in Europe**

Country	Wantai	Abbott	Adaltis	Dia.Pro	Mikrogen	MP	Others
Austria	13.9%	1.9%	0.7%	6.6%	8.9%	3.9%	9.3%
Belgium	19.7%	4.5%	2.5%	10.9%	13.8%	7.4%	19.7%
Czech Republic	12.9%	1.5%	0.5%	5.9%	8.1%	3.3%	12.9%
Denmark	19.8%	4.8%	2.8%	11.4%	14.3%	7.8%	19.8%
France	31.9%	12.0%	8.7%	21.1%	24.7%	16.3%	31.9%
Germany	29.5%	2.6%	1.1%	7.8%	10.3%	4.8%	29.5%
Italy	7.5%	0.1%	0.1%	2.4%	3.9%	0.9%	7.5%
Netherlands	27.0%	1.8%	0.6%	6.4%	8.7%	3.7%	27.0%
Spain	14.7%	2.2%	0.9%	7.1%	9.5%	4.3%	14.7%
Switzerland	21.2%	1.8%	0.6%	4.2%	8.8%	4.2%	21.2%
UK	12.7%	1.4%	0.4%	5.7%	7.9%	3.2%	12.7%

Every year, an estimated 20 million HEV infections occur resulting in more than three million clinical cases and 70,000 deaths. Infected patients show typical serological course, i.e., IgM antibodies appear first, followed by IgG seroconversion. The level of IgM antibodies in the acute phase declines rapidly, then more sustainable IgG antibody are presented for up to 14 years. RNA detection with PCR may also be used for diagnosis of HEV infection. Recently, an anti-HEV antigen (Ag)-specific ELISA have also become commercially available, as an inexpensive alternative to PCR.

**HEV serological and virological courses**



# Wantai HEV-IgG ELISA CE

Wantai HEV IgG kit is an ELISA for qualitative determination of IgG antibodies to hepatitis E virus. It is intended for use in clinical laboratories for diagnosis and management of patients related to infection with hepatitis E virus.

## Clinical sensitivity and specificity

The sensitivity and specificity of Wantai HEV-IgG ELISA were evaluated during multi-center clinical trials conducted in China. Samples from acute hepatitis E, acute non-A, non-B hepatitis, samples from individuals living in hepatitis E outbreak areas, post-infection cases, other hepatitis cases, samples from blood donors, were tested.

**Overall Sensitivity: 99.08%**

**Sensitivity in post-infection samples: 86%**

**Overall Specificity: 99.90%**

### ■ Testing of specimens from general population living in endemic areas

**7258 specimens** from general population were randomly selected from eight counties in China.

**The overall positive rate was 43.3%**



### ■ New infections detection rate:

**3091 individual samples** were collected from endemic areas and followed up for up to one year.

**64 new seroconversion cases** were

observed which was calculated as **3.6%** new infections.

Area	#samples	HEV POS	Infection rate (%)	WT-IgG seroconversions	New infection rate (%)
Lingyu	738	320	66.3	45	6.1
Xingan	533	199	58.6	6	1.1
Luocheng	455	255	41.3	5	1.1
Tiandeng	166	85	37.5	1	0.6
Binyang	657	463	36.3	5	0.8
Lingshan	542	440	24.6	2	0.4
Total	3091	1762	43.0	64	3.6

### ■ Detection of IgG in acute HEV specimens:

In total, **216 specimens** from acute hepatitis E patients with IgM positive results were tested. Wantai HEV-IgG ELISA demonstrated sensitivity of **99.08%**.

Evaluation Centers	No. cases	Wantai IgG		Comparison IgG	
		Positive	Rate	Positive	Rate
Fudan University	98	96	97.96%	90	91.84%
Guangxi CDC	120	120	100.0%	112	93.33%
Total Number	218	216	99.08%	202	92.66%

### Specificity:

**10,587 blood donor specimens** were tested (Beijing Blood Bank, Beijing, China). Wantai HEV-IgG ELISA demonstrated specificity of 99.9%.

# Wantai HEV-IgM ELISA CE



Wantai HEV IgM kit is an ELISA for qualitative determination of IgM-class antibodies to hepatitis E virus. It is intended for use in clinical laboratories for diagnosis and management of patients related to infection with hepatitis E virus.

## Clinical sensitivity and specificity

Samples from 7,113 blood donors, collected in China were tested. Among all blood donors involved in the study, Wantai HEV IgM ELISA detected 124 IgM positive samples (positive rate of 1.74%). All IgM positive results were confirmed by monoclonal antibody blocking assay and/or PCR. Viral RNA was also detected from a single IgM-positive blood donor.

### Comparison against other similar products

#### Sensitivity:

In a performance evaluation study conducted in China, the **sensitivity of Wantai IgM ELISA was 97.10%**. The results were higher result than the sensitivity of the comparison IgM ELISA test (81.5%).

Lab	No.	Wantai HEV IgM		Comparison HEV IgM	
		Pos. No.	Pos. Rate	Pos. No.	Pos. Rate
Hongkong	140	135	96.4%	112	80.0%
Fudan University	48	47	97.9%	35	72.9%
CDC	126	123	97.6%	109	86.5%
<b>Total</b>	<b>314</b>	<b>305</b>	<b>97.1%</b>	<b>256</b>	<b>81.5%</b>



### Comparison against other similar products

#### Specificity:

samples from patients infected with hepatitis A, hepatitis B and hepatitis C viruses, HBV vaccine recipients, patients undergoing routine viral disease testing, blood donors, and healthy individuals. **Specificity of Wantai IgM ELISA was 98.40%.**

#### Specificity for different populations

Testing Centers	Population	Samples	Pos. No.	Specificity (%)
<b>Wantai HEV IgM</b>				
Department of Health, Hong Kong	Acute hepatitis A	168	1	99.4
	Acute hepatitis B	164	1	99.4
	Hepatitis C	168	4	97.6
	HBV vaccine	871	25	97.1
	Population for routine virus testing	445	3	99.3
Fudan University	Healthy individuals	273	0	100.0
	Acute hepatitis A	298	14	95.3
Beijing blood center	Blood donors	7113	124	98.3
Beijing railway hospital	Healthy individuals	883	1	99.9
CDC of Guangxi	Healthy individuals	388	1	99.7
	Blood donors	355	3	99.2
Total	Healthy individuals	9012	129	98.6
	Other populations	2114	48	97.7
<b>Total</b>		<b>11126</b>	<b>177</b>	<b>98.4</b>

#### Testing of potentially interfering samples

Samples	No.	HEV IgM POS	HEV IgM NEG	SPECIFICITY
RF Pos.	48	0	48	100%
Hemoluzed samples	30	0	30	100%
Lipaemic samples	27	0	27	100%
Jaundice, non-HEV samples	31	0	31	100%
Elevated ALT, non-HEV samples	100	0	100	100%
Anti-mouse Ab Pos. human samples	10	0	10	100%
HAV-IgM Ab Pos.	37	0	37	100%
HBc-IgM Ab Pos.	10	0	10	100%
HBV (HBsAg/HBcAb/HBeAg) Pos.	30	0	30	100%
HCV Ab Pos.	40	0	40	100%
HIV Ab Pos.	10	0	10	100%
<b>Total</b>	<b>363</b>	<b>0</b>	<b>363</b>	<b>100%</b>

The results show that there is not interference in Wantai HEV-IgM ELISA.



# Wantai HEV-Ag ELISA<sup>Plus</sup>

WANTAI HEV-Ag ELISA<sup>Plus</sup> is an enzyme-linked immunosorbent assay (ELISA) for the qualitative detection of hepatitis E virus antigen. It is intended for use in clinical laboratories for diagnosis and management of patients related to infection with hepatitis E virus.

## ■ Clinical Specificity

The specificity was determined by testing of **1494 clinical samples** including samples from patients infected with hepatitis A, hepatitis B, hepatitis C and Syphilis; samples from chronic hepatitis patients with unknown nature of infection (AH). **The overall specificity was 99.93%.**

Testing Centers	Samples	Positive (%)	Negative (%)	Total
Center #1	HAV	0 (0%)	36 (100%)	36
	HBV	0 (0%)	40 (100%)	40
	HCV	0 (0%)	40 (100%)	40
	AH	0 (0%)	99 (100%)	99
	<b>Total</b>	<b>0</b>	<b>215</b>	<b>215</b>
Center #2	HBV	0 (0%)	250 (100%)	250
	AH	1 (0.2%)	400 (99.8%)	401
	<b>Total</b>	<b>1</b>	<b>650</b>	<b>651</b>
Center #3	ALT (elevated)	0 (0%)	224 (100%)	224
	TP	0 (0%)	79 (100%)	79
	HBV/HCV	0 (0%)	185 (100%)	185
	<b>Total</b>	<b>0</b>	<b>488</b>	<b>488</b>
Center #4	HAV	0 (0%)	3 (100%)	3
	HBV	0 (0%)	87 (100%)	87
	unknown hepatitis	0 (0%)	50 (100%)	50
	<b>Total</b>	<b>0</b>	<b>140</b>	<b>140</b>
<b>Total</b>		<b>1 (0.07%)</b>	<b>1493(99.93%)</b>	<b>1494</b>



## ■ Clinical Sensitivity

**251 samples** collected from three centers were tested with Wantai HEV-Ag ELISA and the results confirmed by HEV PCR.

**Positive agreement vs. PCR: 66.7%**

**Negative agreement vs. PCR: 95.1%**

Testing Centers	WANTAI	HEV RNA		
Fudan University		+	-	Total
	+	19	4	23
	-	8	162	170
	<b>Total</b>	<b>27</b>	<b>166</b>	<b>193</b>
Beijing You'An Hospital		+	-	Total
	+	11	6	17
	-	7	19	26
	<b>Total</b>	<b>18</b>	<b>25</b>	<b>43</b>
Beijing Red Cross		+	-	Total
	+	0	0	0
	-	0	15	15
	<b>Total</b>	<b>0</b>	<b>15</b>	<b>15</b>
Total		+	-	Total
	+	30	10	40
	-	15	196	211
	<b>Total</b>	<b>45</b>	<b>206</b>	<b>251</b>

# Procedures

Developing Scientifically  
Focusing on the Health

## ■ Wantai HEV-IgM ELISA

Add Diluent	100μl
Add Specimen	10μl
Incubate	30min.
Wash	5times
Add HRP-Conj.	100μl
Incubate	30min.
Wash	5times
Coloring	50μl A+ 50μl B
Incubate	15min.
Stop the reaction	50μl stop solution
Read	450nm or 450/600~650nm

## ■ Wantai HEV-IgG ELISA

Add Diluent	100μl
Add Specimen	10μl
Incubate	30min.
Wash	5times
Add HRP-Conj.	100μl
Incubate	30min.
Wash	5times
Coloring	50μl A+ 50μl B
Incubate	15min.
Stop the reaction	50μl stop solution
Read	450nm or 450/600~650nm

## ■ Wantai HEV-Ag ELISA<sup>Plus</sup>

Add Diluent	20μl
Add Specimen	50μl
Incubate	60min.
Add HRP-Conj.	100μl
Incubate	30min.
Wash	5times
Coloring	50μl A+ 50μl B
Incubate	15min.
Stop the reaction	50μl stop solution
Read	450nm or 450/600~650nm

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WE-7596	HEV-Ag ELISA <sup>Plus</sup>	Antigen	Serum/Plasma	96T/kit