Order information

Product	Material configuration	Material Number
Elecsys® HBeAg quant [a)]	100 tests	09 318 402 190
Elecsys® HBeAg quant [b)]	300 tests	09 318 399 190
PreciControl HBeAg quant [a), b)]	16 × 1.3 mL	09 318 429 190
Diluent Universal 2 [a)]	2 × 36 mL	05 192 943 190
Diluent Universal [b)]	45.2 mL	07 299 001 190

a) for use on **cobas** e 411 analyzer and the **cobas** e 601 / **cobas** e 602 modules; b) for use on the **cobas** e 801 and **cobas** e 402 analytical units

References

1 WHO. [Internet; cited 2023 April] Available from: https://www.who.int/en/news-room/fact-sheets/detail/hepatitis-b.

2 Schweitzer A,et al. Lancet 2015;386(10003):1546-1555.

3 Seeger, C., et al. Hepadnaviruses. In: Knipe DM, Howley RM editors. Field's Virology 5th ed. Lippincott Williams and Wilkins, Philadelphia, USA. 2007;76, 2977-3029.

4 Liaw YF, Chu CM. Lancet 2009;373:582-592.

5 Turgeon ML. Immunology & Serology in Laboratory Medicine, 2013 5th ed, Elsevier Health Sciences, Missouri, USA. Chapter 23.

6 Elgouhari HM, et al. Cleve Clin J Med 2008;75:881-889.

7 Liaw YF. Hepatol Int 2009;3:425-433.

8 Negro F. Swiss Med Wkly 2011;141:w13264.

9 Terrault NA, et al. Hepatology 2018;67(4):1560-1599.

10 WHO. [Internet; cited 2023 April]. Available from: https://www.who.int/publications/i/item/9789241549981.

11 Bleich LM, Swenson ES. J Clin Gastroenterol 2014;48(9):765-772.

12 Park JS, Pan CQ. Hepatol Int 2017;11(6):476-480.

13 WHO. [Internet; cited 2023 April]. Available from: https://www.who.int/publications/i/item/978-92-4-000270-8.

14 Hoofnagle, J.H., et al. Ann Intern Med. 1981;94(6):744-748.

15 Elecsys® HBeAg quant Method Sheet, material number 09318402190 version 09318402500V1.0 and material number 09318399190 version 09318399500V1.0.

16 Kao JH. 2008;2(4):553-562.

17 EASL. J Hepatol. 2017;67(2):370-398.

18 Wong GL, et al. Clin Infect Dis 2016;62(Suppl 4):S298–S305.

19 Fletcher GJ, et al. J Clin Lab Anal 2016;30:1146–1149.

20 Yang HI, et al. N Engl J Med 2002;347:168–174.

21 Mixson-Hayden T, et al. J Clin Virol 2018;109:22–28.

22 Terrault NA, et al. Hepatology 2016;63:261–283.

23 Gao YH, et al. World J Hepatol. 2016;8(34):1511-1520.

24 Wong GL, et al. Clin Infect Dis 2016;62(Suppl 4):S298–S305.

25 Fried MW, et al. Hepatology. 2008;47(2):428-4345.

26 Thompson AJ, et al. Hepatology 2010;51:1933–1944.

27 Bae, SK et al. Med Sci Monit, 2012; 18(12): CR698-705.

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Elecsys® HBeAg quant

Immunoassay for the in vitro qualitative and quantitative determination of hepatitis B e antigen (HBeAg) in human serum and plasma. The assay can be used as an aid for the diagnosis and monitoring of patients with hepatitis B viral infection

Summary
Hepatitis B is a potentially life threatening liver infection caused by the hepatitis B virus (HBV). It is transmitted through contact with blood or other body fluids of an infected person.[1] The disease is not always self limiting: in adults approx. 5 % of acute infections will follow a chronic course of varying degrees of severity; infants will develop chronic hepatitis B in up to 95 % of the cases.[1]

Approximately 300 million people are estimated to be living with HBV Infection. In 2019, hepatitis B resulted in an estimated 820 000 deaths, mostly from cirrhosis and hepatocellular carcinoma (primary liver cancer).[1]

HBeAg is a product of the pre-C/C gene that is found in hepatocytes during proliferation of HBV and is an important diagnostic tool to determine the status of ongoing HBV infections. The detection of HBeAg is generally associated with the presence of large quantities of virus as it is a surrogate of viral replication.[2-4] HBeAg can be detected in serum shortly after hepatitis B s antigen (HBsAg) during acute HBV infections and when the infection is self-limited, usually disappears before HBsAg, when alanine aminotransferase (ALT) levels peak, followed by the presence of the corresponding antibody (anti-HBe).[3-5]

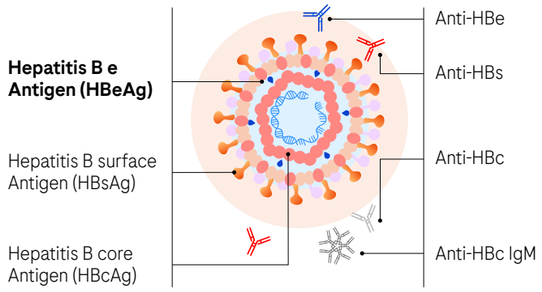
HBeAg can usually be detected when viral replication is high, both in self-limited infections and in chronic hepatitis B; its presence for more than 10 weeks is indicative of a transition to persistent infection. HBeAg seroconversion to anti-HBe suggests the end of active viral replication and is therefore associated with clinical resolution (self-limited) or remission (chronic disease), marking a transition from the immune-active phase of the disease to the inactive carrier state.[3-6]

HBV infections can occur without detectable HBeAg due to infection with HBV variants containing precore stop codon mutants; while the virus can no longer produce HBeAg, disease activity is ongoing and anti-HBe may be present.[3,7,8]

HBeAg seroconversion is a marker for treatment response and a goal of antiviral therapy in HBeAg positive patients.[7,9] As such, quantitative measurement of HBeAg can provide guidance to physicians regarding cessation of antiviral therapy.[10]

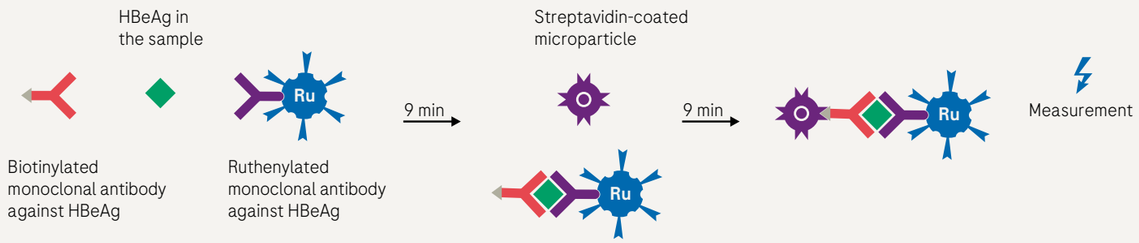
HBeAg is considered an important indicator for risk of mother-to-child transmission[11], where the transmission of HBV from HBeAg positive mothers to newborns plays a significant role.[12] Clinical guidelines recommend to screen all pregnant women with HBeAg serving as a surrogate marker for HBV replication when no access to HBV DNA testing is available.[13]

The Elecsys HBeAg quant test is, therefore, meaningful in association with the anti-HBe test for monitoring the course of HBV infection and the effect of treatment for chronic hepatitis B.[3,4,6,7,13]



Electro-chemiluminescence immunoassay (ECLIA)

Test principle: One-step sandwich assay (testing time: 18 minutes)[15]



Step 1 (9 minutes):

35 µL/21 µL of the patient sample are incubated with monoclonal murine biotinylated and ruthenylated antibodies, both against different HBeAg epitopes.

A sandwich immune complex is formed, with HBeAg carrying a biotinylated and a ruthenylated antibody.

Step 2 (9 minutes):

After the addition of streptavidin-coated paramagnetic microparticles, the sandwich complexes bind to the solid phase via biotin-streptavidin.

Step 3 (measurement):

The reagent mixture is transferred to the measuring cell, where the microparticles are fixed to the electrode surface by magnetic action.

The unbound substances are subsequently removed. Luminescence is then induced by applying a voltage and measured with a photomultiplier.

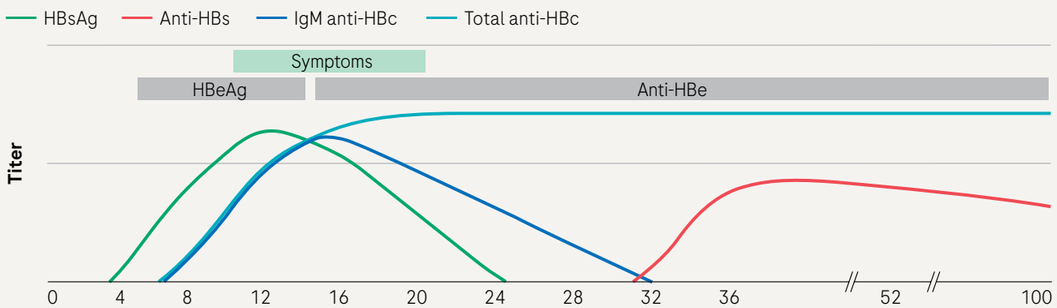
Elecsys® HBeAg quant assay characteristics

Elecsys® HBeAg quant assay characteristics[15]

Systems	**cobas®** e 411 analyzer **cobas®** e 601 / **cobas®** e 602 modules	**cobas®** e 402 / **cobas®** e 801 analytical units
Testing time	18 minutes	
Test principle	One-step sandwich assay	
Calibration	2-point	
Traceability	Standardized against the 1st WHO International Standard Hepatitis B virus e antigen (HBeAg), code 129097/12 of the Paul-Ehrlich-Institut, Langen (Germany).	
Sample material	Serum collected using standard sampling tubes or tubes containing separating gel. Li-heparin, Na-heparin, K_2-EDTA, K_3-EDTA, ACD, CPD, CP2D, CPDA and Na-citrate plasma. Plasma tubes containing separating gel can be used.	
Sample volume	35 µL	21 µL
Reagent Onboard stability	8 weeks	16 weeks
Intermediate precision in positive samples	**cobas** e 411: CV 5.2 – 7.4 % **cobas** e 601/602: CV 6.5 – 9.7 %	**cobas** e 402/801: CV 5.6 – 7.5 %
Limit of Blank	0.05 IU/mL	
Limit of Detection	0.10 IU/mL	
Limit of Quantitation	0.20 IU/mL	
Measuring range	Linear: 0.10 IU/mL - 120 IU/mL	
Extended measuring range	1:20 dilution: 2400 IU/mL	1:30 dilution: 3600 IU/mL
Result interpretation	< 0.23 IU/mL = non-reactive (negative for HBeAg) ≥ 0.23 IU/mL = reactive (positive for HBeAg)	
Relative sensitivity	100 % (310 patients with acute or persistent HBV infection)	
Relative specificity	100 % (routine (n = 1001), blood donors (n = 1000), hospitalized patients (n = 300), dialysis (n = 100) and pregnant women (n = 100))	
Analytical specificity	No cross-reactions with HAV, HCV, HEV, CMV, EBV, HSV, HIV, E. coli, *Toxoplasma gondii*, Rubella and *Treponema pallidum*	

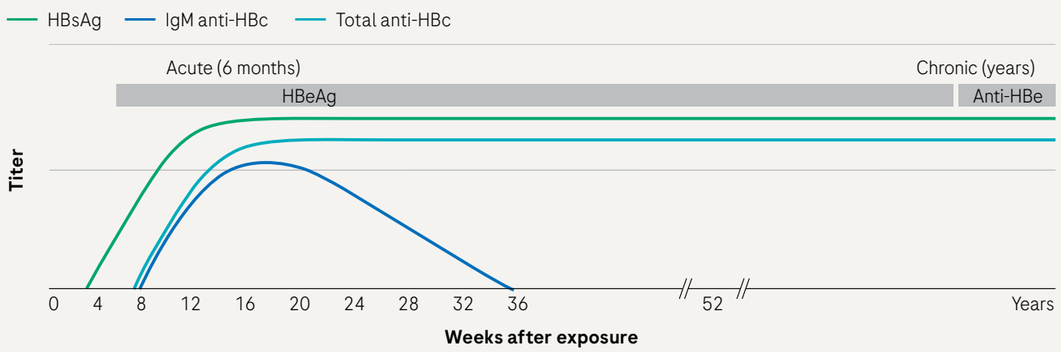
Hepatitis B serologic profiles[16]

Acute Hepatitis B virus infection with recovery



Typical serologic course of an acute hepatitis B virus infection with recovery.

Progression to chronic Hepatitis B virus infection



Typical serologic course of a hepatitis B virus infection with progression to chronic hepatitis B.

Proposed Clinical Use Cases

Critical concentration	Proposed Clinical Use Case	Elecsys® HBeAg	Elecsys® HBeAg quant
≤0.3 IU/mL	To determine whether an individual is HBeAg positive or negative (reactive or non-reactive)	✓	✓
Reactive / non-reactive	To determine the patient's chronic HBV disease phase and predict phase transition(s)[17,18]	✓	✓
Reactive/non-reactive	To assess viral replication[19]	✓	✓
Reactive/non-reactive	To assess the risk of progressive liver disease and HCC[10,20]	✓	✓
Reactive / non-reactive	As a tool in perinatal screening, in particular in resource limited settings[13,22]	✓	✓
Reactive/non-reactive	To monitor antiviral treatment response[7,10,17,18,22]	✓	✓
0.1- 0.3 IU/mL	Quantify HBeAg titers between lower detection limit and medical decision point[15]	✗	✓
~20-30 IU/mL	This level predicts virological response during the continued NA therapy[23,25], and it predicts the activity of the immune system as a marker of responsiveness to therapy and achieving seroconversion to anti-HBe[26]	✗	✓
~100 PEI* / IU/mL	To predict likelihood of seroconversion to anti-HBe or determine non-responders during treatment[25,27]	✗	✓
>2.2 log PEI* / IU/mL	Decline in HBeAg titers at week 24 after start of treatment (NA, INFα) (optimal threshold to predict virological response and HBeAg seroconversion in patients on treatment)[23,24]	✗	✓

* The higher order HBeAg WHO International Standard established in 2013 is a lyophilized preparation of Paul-Ehrlich-Institute standard HBe-Referenzantigen 82, with negligible difference in potency to PEI.
Acronyms: PEI: Paul-Ehrlich-Institute, IU: International Units, NA: Nucleoside analogue, INFα: Interferon-alfa