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Performance evaluation of ExiStation HBV diagnostic system for hepatitis B virus DNA quantitation

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A B S T R A C T

The performance of a recently developed real-time PCR system, the ExiStation HBV diagnostic system, for quantitation of hepatitis B virus (HBV) in human blood was evaluated. The detection limit, reproducibility, cross-reactivity, and interference were evaluated as measures of analytical performance. For the comparison study, 100 HBV-positive blood samples and 100 HBV-negative samples from Korean Blood Bank Serum were used, and the results of the ExiStation HBV system showed good correlation with those obtained using the Cobas TaqMan (r² = 0.9931) and Abbott real-time PCR systems (r² = 0.9894). The lower limit of detection was measured as 9.55 IU/mL using WHO standards and the dynamic range was linear from 6.68 to 6.60 x 10⁹ IU/mL using cloned plasmids. The within-run coefficient of variation (CV) was 9.4%, 2.1%, and 1.1%, and the total CV was 11.8%, 3.6%, and 1.7% at a concentration of 1.92 log10 IU/mL, 3.88 log10 IU/mL, and 6.84 log10 IU/mL respectively. No cross-reactivity or interference was detected. The ExiStation HBV diagnostic system showed satisfactory analytical sensitivity, excellent reproducibility, no cross-reactivity, no interference, and high agreement with the Cobas TaqMan and Abbott real-time PCR systems, and is therefore a useful tool for the detection and monitoring of HBV infection.

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1. Introduction

Hepatitis B is a viral infection that attacks the liver and can cause both acute and chronic liver disease. Two billion people worldwide have been infected with the hepatitis B virus (HBV), and more than 240 million have chronic liver infections. Approximately 600,000 people die every year because of the acute or chronic consequences of hepatitis B (WHO, 2012).

The detection and quantitation of HBV DNA in blood are essential for diagnosis and monitoring of HBV infection, and several methods to detect and quantify HBV DNA have been developed, including hybrid capture assays, bDNA, and real-time PCR. Among these methods, real-time PCR has become the most popular method for quantitation of HBV DNA because of its higher sensitivity and wider dynamic range. The ExiStation HBV diagnostic system used in the present study was designed for the detection and quantitation of HBV DNA extracted from clinical samples such as serum or plasma by using the ExiStation Universal Molecular Diagnostic System.

This study was performed to evaluate the analytical and clinical performance of the ExiStation HBV diagnostic kit (ExiStation Viral DNA Extraction kit and AccuPower HBV Quantitative PCR kit, Daejeon, Korea) to detect HBV in human blood by using the recently developed ExiStation Universal Molecular Diagnostic System.

2. Materials and methods

2.1. Standards

The 3rd WHO International Standard for Hepatitis B Virus for Nucleic Acid Amplification Techniques (NIBSC Code 10/264, National Institute for Biological Standards and Control, Hertfordshire, UK) in lyophilized plasma was used for determination of the lower limit of detection (LOD). A standard panel of plasma samples (Worldwide HBV DNA performance panel; WWHD301-01-20; Negative, Genotype A, B, C, D, E, F, G, and H; Seracare Life Sciences, Milford, USA) was used to determine the LOD of the assay according to genotype.
2.2. Clinical samples for comparison study

For the comparison study with the Abbott real-time PCR assay and Roche Cobas TaqMan real-time PCR assay, 100 HBV DNA-positive blood plasma samples and 100 HBV DNA-negative blood plasma samples were obtained from the Human Serum Bank of the Korea National Research Resource Center (http://knrcb.knrc.or.kr). HBV genotype for HBV DNA-positive plasma samples was determined by direct sequencing of the polymerase gene with BLAST analysis and alignment with sequences in GenBank. These 100 HBV DNA-positive blood plasma samples were all genotype C, which is the predominant genotype in Korea.

2.3. ExiStation HBV diagnostic system

The ExiStation HBV diagnostic system uses real-time PCR technology for quantitative detection of HBV DNA in human serum. The ExiStation consists of three ExiPrep 16 Dx nucleic acid extraction instruments and one Exicycler 96 real-time quantitative thermocycler, which allow handling of up to 48 individual clinical specimens per run. ExiStation manager software controls the entire process of nucleic acid preparation, amplification and automatic data acquisition and analysis, and finally delivers a report to the user. The ExiPrep 16 Dx automates the extraction and purification of nucleic acids from clinical specimens by utilizing magnetic particle technology. All reagents for extraction are included in the cartridge of the ExiStation viral DNA extraction kit. Extracted DNA is eluted into diagnostic reaction tubes directly, and therefore, real-time PCR on the Exicycler 96 is performed without a manual pipetting step.

DNA in a 400-μL serum sample was extracted using the ExiStation viral DNA extraction kit and the ExiPrep 16 Dx of the ExiStation Universal Molecular Diagnostic System (Bioneer, Daejeon, Korea). The extracted HBV DNA was automatically loaded into the quantitative PCR tubes, and real-time PCR was performed by a PCR cycler (Exicycler 96 Real-Time Quantitative Thermal Block of the ExiStation Universal Molecular Diagnostic System, Bioneer, Daejeon, Korea) with the following program: pre-denaturation at 95 °C for 5 min, followed by 45 cycles of denaturation at 95 °C for 5 s and annealing/extension at 55 °C for 5 s. All procedures were conducted according to the manufacturer's instructions. The concentration of HBV DNA in a sample was determined on the basis of the Ct value, and the corresponding concentration (IU/mL) of DNA was extrapolated from standard curves. An internal positive control consisting of DNA sequences unrelated to the HBV target sequence, was pre-loaded in each sample loading tube from the beginning of DNA extraction from specimens to determine whether the nucleic acids were properly extracted and amplified in each reaction and whether PCR was inhibited by the sample.

2.4. Abbott real-time PCR system and Roche Cobas TaqMan real-time PCR system for comparison study

For the Abbott real-time PCR system, DNA extracts were prepared from 500-μL plasma samples by using a m2000sp automated sample preparation system that utilizes magnetic microparticles. Amplification was conducted in the Abbott m2000rt system, and that HBV DNA concentration was calculated using the calibrators provided with the kit. For the Roche Cobas TaqMan real-time PCR system, DNA was extracted from 650-μL of plasma by using the Cobas AmpliPrep automated extractor according to the manufacturer's instructions. The Cobas Taqman 48 analyzer was used for amplification and detection of PCR products according to the manufacturer’s instructions.

2.5. Lower limit of detection (LOD)

To determine the LOD, the 3rd WHO International Standard for Hepatitis B Virus for Nucleic Acid Amplification Techniques (National Institute for Biological Standards and Control; NIBSC Code 10/264) was used. Lyophilized plasma was reconstituted in 0.5 mL of nuclease-free water. The reconstituted plasma with a final concentration of 850,000 IU/mL was diluted serially in human plasma negative for HBV, HCV, and HTLV (AcroMetrix® EDTA Plasma Dilution Matrix, AcroMetrix Corporation, Benicia, CA, USA), and the diluted HBV DNA concentrations of 1000, 333.3, 111.1, 37.0, 12.3, 4.1, 1.03, and 0.52 IU/mL were used to determine the LOD of the assays. Twenty-four replicates for each HBV DNA concentration were tested, and the proportion of positive results obtained from each concentration was subjected to probit regression analysis.

To determine the LOD according to genotype, a standard panel of plasma samples (Worldwide HBV DNA Performance Panel WWHD301; Genotype A, B, C, D, E, F, G, and H) was used. Each target region of each genotype of the panel was amplified, and the amplicon was cloned into a pGEM-T easy vector (PROMEGA, Madison, WI, USA) and then transformed into HIT-DH5α competent cells (RBC Bioscience, New Taipei City, Taiwan). The cloned plasmid was purified using an AccuPower plasmid mini kit (Bioneer Co., Korea), and the amount of purified plasmid was measured using a NanoDrop 2000 (Thermo Fisher Scientific, Wilmington, DE, USA) and converted to a copy number. The absolute number of hepatitis B virus genomes in a sample was determined based on the Ct (cycle threshold) value, where the number of DNA copies was extrapolated from calibration curves. The cloned plasmid was diluted serially in human plasma, and 24 replicates of each HBV DNA concentration of 222.6, 74.2, 24.7, 8.2, 2.7, and 0.91 IU/mL were tested. The proportion of positive results obtained from each concentration was subjected to probit regression analysis to determine the LOD.

2.6. Dynamic range

To examine the dynamic range of the ExiStation HBV diagnostic system, serial dilutions of the cloned plasmid standards ranging from 10 to 10^10 copies/reaction (6.68–6.68 × 10^9 IU/mL) were generated, and 8 replicates each of 10 dilutions were tested.

2.7. Repeatability/reproducibility

Three HBV-positive serum samples with different viral loads and 1 HBV-negative serum sample were tested in triplicate, with 1 run per day over a period of 20 days. The within-run coefficient of variation (CV) and total CV were calculated.

2.8. Assessment of equal quantitation in serum and plasma

Blood samples from 25 HBV-positive patients and 25 HBV-negative patients were collected using SST tubes, EDTA tubes, and citrate tubes (Becton Dickinson and Company, USA). All serum samples in SST tubes and plasma samples in EDTA tubes and citrate tubes were tested in parallel using the ExiStation HBV diagnostic system.

2.9. Cross-reactivity

Cross-reactivity with the following viruses was examined using the virus culture supernatant; rotavirus (ATCC VR-2018 from American Type Culture Collection), adenovirus type 40 (ATCC VR-931), type 41 (ATCC VR-930), type 31 (ATCC VR-1109), type 11 (ATCC VR-12), type 8 (ATCC VR-1604), type 37 (ATCC VR-929), type 1 (KBVP-VR-57 from Korean Bank for Pathologic Viruses),
type 2 (KBPV-VR-58), type 3 (KBPV-VR-2), type 4 (KBPV-VR-60), type 8 (KBPV-VR-3), type 18 (KBPV-VR-4), type 23 (KBPV-VR-5), enterovirus type 71 (ATCC VR-784), cytomegalovirus (ATCC VR-538), polyvirus type 1 (ATCC VR-58), coxsackievirus A type 9 (ATCC VR-186), coxsackievirus B type 3 (ATCC VR-688), coxsackievirus B type 5 (ATCC VR-1036), coxsackievirus B type 6 (ATCC VR-1037), BK virus (ATCC VR-837), herpes simplex virus type 1 (ATCC VR-733), respiratory syncytial virus (ATCC VR-26), parainfluenza virus type 2 (ATCC VR-92), parainfluenza virus type 3 (ATCC VR-93), rhinovirus type 14 (ATCC VR-284), echo virus type 7 (ATCC VR-37), coronavirus (ATCC VR-740, -759), and mumps virus (ATCC VR-106).

2.10. Interference testing

Interference testing was performed to determine whether potential interfering substances affected the HBV assay results. Samples that were weakly positive or negative for HBV and contained a high concentration of interfering substances or no interfering substances were tested using similar procedures. All interfering substances were purchased from Sigma–Aldrich Co., USA except for K₂ EDTA (Becton Dickinson, Franklin Lakes, NJ, USA). The total concentrations of the interfering substances were K₂ EDTA (540 mg/dL), citrate (0.327 M), heparin (3 IU/dL), hemoglobin (200 mg/dL), cholesterol (500 mg/dL), albumin (5 g/dL), and bilirubin (25 mg/dL).

The 3rd WHO International Standard for Hepatitis B Virus (National Institute for Biological Standards and Control, Hertfordshire, UK) was used as an HBV-positive sample. HBV-positive samples were prepared at a concentration of 30 IU/mL by diluting the HBV DNA standard in human normal serum (Millipore, Billerica, MA, USA). Interference testing was also performed using HBV-negative samples to determine the influence of interfering substances on negative results. Four replicates were tested for each substance.

2.11. Statistical analysis

HBV DNA concentrations were log₁₀ transformed for analysis. The LOD was determined as the 95% probability of obtaining a positive HBV DNA result. Probit regression analysis was performed to determine the LOD. For the repeatability/reproducibility test, the within-run precision and total precision were expressed as coefficient of variation (CV). For the comparison study, linear regression analysis and the Bland–Altman plots were performed to measure the correlation and agreement among the assays. The Friedman test was applied to determine the equality of HBV DNA quantitation among 3 different tubes.

3. Results

3.1. Analytical sensitivity (lower limit of detection)

To determine the LOD, the serial dilutions of the WHO standard of HBV DNA (NIBSC) at concentrations of 1000, 333.3, 111.1, 37.0, 12.3, 4.1, 1.03, and 0.52 IU/mL were tested in 24 replicates. Twenty-four replicates containing HBV DNA at concentrations of 1000, 333.3, 111.1, and 37.0 IU/mL were positive on ExiStation HBV diagnostic system. One of the 24 replicates at 12.3 IU/mL, 4 out of the 24 replicates at 4.1 IU/mL, 14 out of the 24 replicates at 1.03 IU/mL, and 19 out of the 24 replicates at 0.52 IU/mL were negative for HBV DNA on real-time PCR. The probit analysis showed that the LOD for ExiStation HBV diagnostic system was 9.55 IU/mL (95% confidence interval: 4.68–19.50 IU/mL) (Table 1).

Table 1

Limit of detection of the ExiStation HBV diagnostic system.

| NIBSC standard HBV DNA concentration (IU/mL) | Positive No. (%) of replicates (n=24) |
|---------------------------------------------|---------------------------------------|
| 1000                                        | 24 (100)                              |
| 333.3                                       | 24 (100)                              |
| 111.1                                       | 24 (100)                              |
| 37.0                                        | 24 (100)                              |
| 12.3                                        | 23 (95.8)                             |
| 4.1                                         | 20 (83.3)                             |
| 1.03                                        | 10 (41.6)                             |
| 0.52                                        | 5 (20.8)                              |

Detection limit by probit analysis: 9.55 IU/mL (95% confidence interval: 4.68–19.50 IU/mL).

Genotype E, 4.6 IU/mL for Genotype F, and 38 IU/mL for Genotype H. However, genotype G could not be cloned, and therefore, the LOD for Genotype G could not be obtained.

3.2. Dynamic range

Serial dilutions of the cloned plasmid standard ranging from 10 to 10¹⁰ copies/reaction (6.68–6.68 × 10⁸ IU/mL) were obtained, and each dilution was measured 8 times. A linear relationship was obtained between the measured Ct values and the log₁₀ concentration of the HBV DNA (y = −3.01x + 40.54, r² = 0.9960, P < 0.001) (Fig. 1).

3.3. Repeatability and reproducibility

The repeatability and reproducibility of the assays were evaluated based on within-run variation, between-day variation, and total variation determined using 3 different concentrations of HBV DNA-positive samples and a negative sample. Sixty measurements of the negative samples obtained over 20 days all showed negative results. The within-run coefficient of variation (CV) was 9.4%, 2.1%, and 1.1% at a concentration of 1.92 log₁₀ IU/mL (98.9 IU/mL), 3.88 log₁₀ IU/mL (7.94 × 10³ IU/mL), and 6.83 log₁₀ IU/mL (7.14 × 10⁶ IU/mL), respectively. The total CV was 11.8%, 3.6%, and 1.7% at the same concentrations, respectively (Table 2).

3.4. Comparison with the results of other real-time PCR systems

One hundred HBV-positive samples were all positive and 100 HBV-negative samples were all negative in the 3 different real-time PCR assays. These positive and negative samples were all genotyped and confirmed by the Human Serum Bank at the Korea National Research Resource Center (http://knrrb.knrcc.or.kr). Therefore, the

![Fig. 1. Dynamic range of the ExiStation HBV diagnostic system. One copy/reaction was equivalent to 0.668 IU/mL.](image-url)
sensitivity and specificity of the real-time PCR assay were regarded to be 100% (95% confidence interval: 96.4–100%). For positive samples, there was a significant relationship between the HBV DNA levels obtained by the Bioneer ExiStation and Abbott real-time PCR systems ($r^2 = 0.9854$), and between those obtained by the Bioneer ExiStation and Roche Cobas TagMan real-time PCR systems ($r^2 = 0.9931$) (Figs. 2 and 3). A Bland–Altman plot was used to determine the agreement among systems. A slight overestimation of HBV DNA levels by the Bioneer ExiStation PCR system was detected relative to the Roche Cobas TagMan and Abbott PCR systems. The mean difference between the Bioneer and Roche systems was 0.11 log$_{10}$ IU/mL, and the mean difference between the Bioneer and Abbott systems was 0.20 log$_{10}$ IU/mL (Figs. 2 and 3).

### 3.5. Assessment of equal quantitation in serum and plasma

No statistically significant differences in HBV DNA levels were found among the 3 types of tubes (SST tube, EDTA tube, and citrate tube) (Table 3).

### 3.6. Cross-reactivity

No cross-reactivity was observed for any of the 30 viruses (see Section 2 for details).

### 3.7. Interference

No interference was observed for K$_2$ EDTA, citrate, heparin, hemoglobin, cholesterol, and bilirubin. The mean HBV concentration evaluated from samples weakly positive for HBV DNA with no interfering substances was 26.34 IU/mL (1.42 log$_{10}$ IU/mL). No reduction or enhancement in performance was observed in the presence of interfering substances for all samples that were weakly positive or negative for HBV DNA (Table 4).

### 4. Discussion

In this study, the detection limit, dynamic range, repeatability/reproducibility, cross-reaction, and interference of the Bioneer ExiStation HBV diagnostic system for quantitation of HBV DNA were evaluated and the results for patients’ samples obtained using the ExiStation HBV diagnostic system were compared with those obtained using other HBV real-time PCR systems.

The detection limit for the ExiStation HBV diagnostic system using the WHO international standard was 9.55 IU/mL, which was lower than or similar to that of other real-time PCR systems (Artus-DB, 82 IU/mL; Artus-DSP, 91 IU/mL; Abbott, 1.43 IU/mL; Roche TaqMan, 12 IU/mL; new real-time PCR, 22.2 IU/mL) (Ismail et al., 2011; Caliendo et al., 2011; Chevaliez et al., 2010). The Bioneer ExiStation HBV diagnostic system was able to detect HBV DNA at a concentration lower than 10 IU/mL and meet the recommended

### Table 2

|          | Mean (log$_{10}$ IU/mL) | Within-run SD (log$_{10}$ IU/mL) | Within-run CV (%) | Between-day SD (log$_{10}$ IU/mL) | Between-day CV (%) | Total SD (log$_{10}$ IU/mL) | Total CV (%) |
|----------|-------------------------|----------------------------------|-------------------|-----------------------------------|-------------------|-----------------------------|--------------|
| Not detected | 1.92                     | 0.18                             | 9.4               | 0.14                              | 7.1               | 0.22                        | 11.8         |
|          | 3.88                     | 0.08                             | 2.1               | 0.11                              | 2.9               | 0.14                        | 3.6          |
|          | 6.84                     | 0.07                             | 1.1               | 0.09                              | 1.3               | 0.12                        | 1.7          |

Fig. 2. Correlation of HBV DNA levels obtained using the ExiStation HBV diagnostic system with those obtained using the Abbott real-time PCR system.

Fig. 3. Correlation of HBV DNA levels obtained using the ExiStation HBV diagnostic system with those obtained using the Roche Cobas TaqMan real-time PCR system.
Table 3  
Differences among blood collection tubes in the ExiStation HBV diagnostic system.

| Samples                               | Mean value of HBV DNA in SST tubes (log_{10} IU/mL) | Mean value of HBV DNA in EDTA tubes (log_{10} IU/mL) | Mean value of HBV DNA in citrate tubes (log_{10} IU/mL) |
|---------------------------------------|----------------------------------------------------|------------------------------------------------------|-------------------------------------------------------|
| HBV DNA positive samples (n = 25); median (25th percentile, 75th percentile) | 2.840 (1.929, 3.908)* | 3.039 (2.252, 3.872)* | 2.881 (2.384, 3.808)* |
| HBV DNA negative samples (n = 25)     | ND                                                 | ND                                                   | ND                                                   |

ND, not detected.  
* No significant differences among three groups by Friedman test.

Table 4  
Interference test of the ExiStation HBV diagnostic system.

| Samples                | Mean of HBV DNA concentration in HBV-positive sample without interfering substance (n = 10) (log_{10} IU/mL) | Mean of HBV DNA concentration in HBV-positive sample with interfering substance (n = 4) (log_{10} IU/mL) | P-value* | Mean of HBV DNA concentration in HBV-negative sample without interfering substance (n = 4) (log_{10} IU/mL) | Mean of HBV DNA concentration in HBV-negative sample with interfering substance (n = 4) (log_{10} IU/mL) |
|------------------------|-------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|----------|---------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|
| K2 EDTA (540 mg/dL)    | 1.42                                                                                           | 1.54                                                                                           | NS       | ND                                                                                                                               | ND                                                                                                                               |
| Citrate (0.327 M)      | 1.42                                                                                           | 1.53                                                                                           | NS       | ND                                                                                                                               | ND                                                                                                                               |
| Heparin (3 kU/dL)      | 1.42                                                                                           | 1.40                                                                                           | NS       | ND                                                                                                                               | ND                                                                                                                               |
| Hemoglobin (200 mg/dL) | 1.42                                                                                           | 1.43                                                                                           | NS       | ND                                                                                                                               | ND                                                                                                                               |
| Cholesterol (500 mg/dL)| 1.42                                                                                           | 1.48                                                                                           | NS       | ND                                                                                                                               | ND                                                                                                                               |
| Albumin (5 g/dL)       | 1.42                                                                                           | 1.27                                                                                           | NS       | ND                                                                                                                               | ND                                                                                                                               |
| Bilirubin (25 mg/dL)   | 1.42                                                                                           | 1.29                                                                                           | NS       | ND                                                                                                                               | ND                                                                                                                               |

NS, not significant; ND, not detected.  
* P-value by independent t-test between HBV positive samples without and with interfering substances.

guidelines suggested by the European Association for the Study of the Liver (less than 10 IU/mL) (EASL, 2009). Linearity was maintained from 10 to 10^{10} copies/reaction (6.68–6.86 × 10^9 IU/mL) (Fig. 1).  
The LOD was 7 IU/mL for Genotype A, 22 IU/mL for Genotype B, 16 IU/mL for Genotype C, 26 IU/mL for Genotype D, 20 IU/mL for Genotype E, 4.6 IU/mL for Genotype F, and 38 IU/mL for Genotype H. Therefore, it was confirmed that the ExiStation HBV diagnostic system was able to detect Genotypes A, B, C, D, E, F, and H. Because Genotype G could not be cloned in this study, the detectability for Genotype G was not determined.  
The within-run CV and between-day CV over 20 days were less than 10%, and the total CV at concentrations of 1.92 log_{10} IU/mL, 3.88 log_{10} IU/mL, and 6.84 log_{10} IU/mL was 11.8%, 3.6%, and 1.7%, respectively. Because a DNA concentration of 1.92 log_{10} IU/mL (82.3 IU/mL) is very low, the total CV of 11.8% observed at this concentration can be regarded as acceptable precision.  
The comparison of clinical samples showed that the 100 HBV-positive samples were all positive and 100 HBV-negative samples were all negative in the 3 different real-time PCR assays, and this finding indicates a 100% agreement rate among the 3 PCR systems and that the sensitivity and specificity of the ExiStation real-time PCR assay was 100% (95% confidence interval: 96.4–100%). Although levels detected by the ExiStation PCR system for the 100 positive samples were slightly higher than those detected by the Roche and Abbott PCR system, they showed good correlation with the levels obtained using the Abbott and Roche PCR systems. The mean difference was 0.2 log_{10} IU/mL or lower.  
The influence of anticoagulants and vacutainer tubes on HBV real-time PCR results in this study was negligible, and there were no statistically significant differences in HBV DNA levels among the 3 types of tubes. There have been several reports regarding the effect of anticoagulants on PCR. Heparin inhibited detection of hepatitis B virus DNA by PCR (Pardoe and Michalak, 1995) and inhibited detection of HCV genomes in serum (Manzin et al., 1994; Furuwataro et al., 1998). However, other studies have indicated the absence of any inhibitory effect of anticoagulants in the amplification of CMV DNA (Storch et al., 1994), as well as a lack of difference in results obtained using plasma samples and serum (Boom et al., 1999). These differences from study to study may be the result of the type of Taq DNA polymerase used, the number of leukocytes present in the blood, or the concentration of heparin in the samples (García and Blanco, 2002).  
Cross reactions with other viruses did not occur, and no interference was introduced by high concentrations of K2 EDTA, citrate, heparin, hemoglobin, cholesterol, albumin, or bilirubin, which are potentially interfering substances present in anti-coagulant blood collection tubes or patients’ blood.  
In conclusion, the ExiStation HBV diagnostic system showed excellent analytical sensitivity and reproducibility, as well as no cross-reactivity, no interference, and high agreement with the Roche Cobas TaqMan system and Abbott real-time PCR system. These findings indicate that the ExiStation HBV diagnostic system is a reliable tool for the detection and monitoring of HBV infection.

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