

July 31, 2017

Dear Editor:

Please find the revised manuscript in Word format (file name: 34721-Revised manuscript).

Name of Journal: World Journal of Gastroenterology

Manuscript NO: 34721

Title: Performance Verification and Comparison of TianLong Automatic Hypersensitive HBV DNA Quantification System with Roche CAP/CTM System

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The manuscript has been improved according to the suggestions of the reviewers and the editor.

1. Format has been updated.
2. Revision has been made according to the suggestions of the reviewers.

Reviewer's code: 02528812

Comments:

- 1) There needs to be a space between some words. This should be checked throughout.

Answer:

The format of the manuscript has been updated carefully.

- 2) I would recommend a linguistic revision of the manuscript by a native speaker as some parts do not read very well.

Answer:

The language of the manuscript has been revised and got a language editing certificate.

Reviewer's code: 01564209

Comments:

- 1) English style, punctuation, typing and grammar needs strong attention and should be checked carefully best by a native English speaker.

Answer:

The language of the manuscript has been revised and got a language editing certificate.

2) Introduction section, 2nd para. What is a “high barrier resistant gene drug”? In my opinion it is “an antiviral drug with a high genetic barrier to resistance”. Please correct this.

Answer:

This has been corrected in "Introduction section, 2nd para." as below.

"During the last decade, with the advent of new type interferon and antiviral drugs with a high genetic barrier to resistance, the antiviral treatment of chronic HBV infection has achieved significant progress."

3) Introduction, 2nd para. What is a “sensitive quantitative reagents”? Do you mean “NAT systems”?

Answer:

Yes. This has been corrected in "Introduction section, 2nd para." as below.

"Use of hypersensitive HBV DNA quantification system to accurately detect HBV DNA in serum is the key factor in determining the curative effect and endpoints of hepatitis B antiviral therapy."

4) Results and Discussion section. The colleagues argued that there are no international universal standard for HBV DNA PCR. This is not correct. Please refer to: WHO International Standard “3rd WHO International Standard for Hepatitis B Virus for Nucleic Acid Amplification Techniques (NIBSC code: 10/264). As a suggestion, the involvement of the WHO standard may enhance the impact of this study.

Answer:

The reviewer is right about International Standard. Unfortunately, we had not enough international standard samples for analytical performance verification. So national standard materials for HBV serum were used to verify the assay performance including accuracy, limit of detection and limit of quantification. And we used the standard from the NCCL of China. The wrong sentence has been deleted.

5) With regard to the clinical samples, were the serum samples tested for co-infections with HIV, HCV, HDV etc? Please note this in the Material and Method section.

Answer:

This has been added in the "Clinical samples" section as below.

" The clinical serum samples were tested for co-infections with HIV, HCV and HDV. All results were negative."

6) Discussion section, 1st para, 1st sentence. It is “HBV includes..” not “genes” (make no sense). Must also A “-” I not “A ~ I”, and most important A -I are genotypes not subtypes. The wrong term Subtypes instead of Genotypes was used also at other places in the text and should corrected.

Answer:

The wrong term Subtypes and "A~I" has been corrected to Genotypes and "A-I" throughout the manuscript.

7) To show accuracy of the quantitative tests of the TL system a representative plot as a figure would be helpful for the readers.

Answer:

In clinical performance test of 200 samples, we used representative plot as a figure to show accuracy of the TL system. In the evaluation of accuracy, we used a table (Table 4) to show the results because there were few data points.

8) Table 4 has no additional validity and was described in the results text. Therefore Table 4 can be omitted.

Answer:

Yes. Table 4 has been deleted.

9) Table 5. is not clear to me and seems to be unnecessary.

Answer:

Yes. Table 5 has been deleted.

10) Is the TL system available outside of China?

Answer:

TL system is not available outside of China today. We hope to make it happen in 2018.

Reviewer's code: 00004603

Comments:

This paper is very technical, it is far from considering as a basic study and should be submitted to a special Journal. This is not the matter of the manuscript quality, just in the journal that deals with technology it will be more appreciated.

Answer:

We hope this manuscript will be helpful.

Reviewer's code: 02528622

Comments:

Minor grammatical can be found spread throughout the paper. A review of the style in some sections of the manuscript will likely improve the paper facilitating reading.

Answer:

The language of the manuscript has been revised and got a language editing certificate.

Reviewer's code: 02942798

Comments:

1) Discussion needs improvement, please add references to discussion and compare TL AH HBV DNA quantification system with other systems using in laboratory practice.

Answer:

A comparative paragraph of TL system and other systems has been added as below.

"Qiu N. et al reported a comparison of the Abbott and Da-an real-time PCR for the quantitation of serum HBV DNA[13]. The Abbott assay had a higher sensitivity, shorter assay time, and

wider dynamic range compared with the Da-an assay. However, the costs of the Abbott assay limited its routine use in clinical molecular laboratories in China. The clinical performance of the TL system was comparable to the CAP/CTM system, with reasonable costs."

2) Please edit references by the rules used in World journal of gastroenterology.

Answer:

The references have been edited by the rules.

3) Add authors contribution, conflict of interests and funding.

Answer:

The authors contribution, conflict of interests have been added follow the editor's instruction.

4) Papers needs a linguistic revision of the manuscript by a native speaker.

Answer:

The language of the manuscript has been revised and got a language editing certificate.

3. References and typesetting were corrected.

Authors appreciate very much for the editor's revision and reviewers' comments, and hope that with these additions and modifications to the manuscript you will find it acceptable for publication in the *World Journal of Gastroenterology*.

Sincerely yours,



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