Format for ANSWERING REVIEWERS

November 25th, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6513-review.doc).

Title: Management of chronic hepatitis B infection: Current treatment guidelines, challenges, and new developments

Author: Ceen-Ming Tang, Tung On Yau, Jun Yu

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 6513

The manuscript has been improved according to the suggestions of reviewers:
1. Format has been updated

2. Revision has been made according to the suggestions of the reviewer.

I. The classification of drugs as nucleos(t)ide analogues, or immunomodulatory agents has been made more prominent within the text. The mechanism of interferons, and nucleos(t)ide analogues are also now included.

II. Guidelines from AASLD and EASL are included in the manuscript, most noticeably in the tables. This has now been made clear in the figure legends.

III. Cirrhosis has now been included as one of the sequelae of chronic HBV infection

IV. On page 3, line 15, the sentence has now been rephrased to: "… therapies of finite duration using immunomodulators such as standard or pegylated interferon-α

V. The annual rate of HBeAg seroconversion and clearance is dependent on factors including an individual's age at acute infection. The following phrase has been added for clarity: "Where 80 to 90% of infants infected will develop chronic infections, less than 5% of otherwise healthy adults who are infected will fail to spontaneously resolve an acute infection."

VI. On page 7, the use of HBsAg levels as a predictor of treatment response is now mentioned.

VII. On page 11, the correct designation of IL28B is now used.

VIII. On page 11, the SNP locations for each genotype reference has been added to prevent confusion over the alleles given.

IX. Text has been modified to clarify that prolonging treatment with PEG-IFN to 96 weeks does not increase adverse effects.

X. If used sequentially, patients resistant to lamivudine are more likely to also be resistant to adefovir. However, in a treatment-naïve population, the risk of resistance on combination therapy with lamivudine and adefovir is low. Hence it may be used with similar efficacy compared to entecavir or tenofovir in resource poor settings.

XI. Spelling correction: "rationale" to "rational"

XII. Table 1 has been corrected. The geographical distribution of genotype F has been changed to "South America". The geographical distribution of genotype D has also been amended to "Southern Europe, North Africa, Middle East, Indian Sub-Continent". It is not possible to explain genotypes E to H in more detail due to a lack of published data.

XIII. The title for Table 7 has been amended to "Treatment Endpoints in Clinical Use" for clarity.

XIV. The title for Table 8 has been amended to "Emerging pipeline drugs for chronic HBV infection" for clarity. Drugs which have been abandoned within the last few years (e.g. pradefovir) are included in the table to inform the reader that no further clinical trials are planned.

XV. In Table 9, the second column ("Trial Name") lists the http://clinicaltrials.gov/ identifier. This table lists several promising clinical trials, which may change the principles of management.

XVI. Figure legends for all diagrams are now included.

XVII. Figure legends for tables are now included where appropriate.

3. References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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