To:

Dr Fang-Fang Ji,

Scientific Editor

We are submitting for consideration for publication in your distinguished journal the revised manuscript 33104 entitled: "The evolving role of Sorafenib in the management of hepatocellular carcinoma". First and foremost, we would like to thank the reviewers and the scientific editor of the journal, Dr Fang-Fang Ji, for taking the time and effort to assess our initial manuscript so meticulously. We took into account all of your recommendations and modified our manuscript accordingly. Detailed replies to the reviewer's comments are provided below:

Reviewer 00742507:

"Interesting and well-written state-of-the-art review of current knowledge of the use of Sorafenib in treatment of hepatocellular cancer. The paper represents an important contribution to this field."

-Thank you for your time and effort in thoroughly evaluating our work and for your acceptance.

Reviewer 02445450:

"This review provides a timely and comprehensive information on sorafenib-related treatments for HCC, together with currently used guidelines. Also, this manuscript states future development of promising small molecules for HCC therapy."

-We are thankful for your comments, as well as your acceptance.

Reviewer 03699981:

"Good for publication and extensive review Need to add "inhibitors" in page 14, line

9 (sorafenib and HIF-1A inhibitor?) Also, in page 16 (line 1, line 10) and page 17

(line 10)"

-We would like to thank you for your indications and acceptance. We made

sure to incorporate the appropriate changes in the manuscript.

Reviewer 03659723:

"In the described review, the author has highlighted the current status of Sorafenib's

mono-and combined therapies, which is the only approved new targeted drug for

systemic treatment of hepatocellular carcinoma, especially for advanced tumor stage.

The aim of the described review is clear. Finally, the described review requires English

language copy edited prior to publication."

-We really appreciate your comments and are thankful for your time. One of

the authors is a native speaker Nevertheless, we made sure to check again the

manuscript for possible language-related flaws and misunderstandings.

Sincerely yours,

Georgios Tsoulfas, MD, PhD, FICS, FACS

Assistant Professor of Surgery

Aristotle University of Thessaloniki, School of Medicine, Thessaloniki, Greece

Tel:+306971895190

Email: tsoulfasg@gmail.com