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05/01/2014

Re: Revision of **ESPS Manuscript NO: 6307**

Dear Lian-Sheng Ma,

Please find enclosed the edited manuscript in Word format (file name: **ESPS Manuscript NO- 6307-Review.doc**).

Title: Controversies in the Pathological Assessment of Colorectal Cancer

Authors: Aoife Maguire and Kieran Sheahan

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 6307

The suggestions of the reviewers have been incorporated into the revised manuscript. The responses to the reviewers comments are outlined below.

REVIEWER 00004093

This reviewers comments have been addressed in an additional section on pages 19 and 20 of the manuscript, highlighted in yellow.

Comment 1: I request the authors to discuss (maybe by adding just a few more sentences) a rapidly increasing role of molecular pathology assessment (which is now a part of pathology assessment) in clinical practice and epidemiology.



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Response: A short section on molecular pathology has been added.

Comment 2: Please discuss a recent study by X Liao et al. N Engl J Med 2012.

Response: The study by Liao et al has been referenced (reference 120).

Comment 3: Please also refer to molecular biomarker guidelines by NCCN (P Febbo et al. JNCCN 2011).

Response: The NCCN molecular biomarker guidelines have been referenced (reference 121).

REVIEWER 00058510

Comment 1: Minor amendments are recommended in the section on peritoneal involvement to reflect that UK pathologist continue to use TNM 5. Use of TNM 7 for T4a and T4b needs to be stipulated as these are different in TNM 5.

Response: This explanation has been added in a new paragraph on page 3 of the manuscript, highlighted in yellow.

Comment 2: The title of "Controversies in" negates the need to be all encompassing, but I wonder if a short section/analysis on perineural invasion would be relevant in such a valuable reference paper.

Response: A section on perineural invasion has been added on pages 14 and 15 of the manuscript, highlighted in yellow.

Comment 3: The other obvious controversy worth considering would be the issue of lymph node sampling, clearing, numbers etc but this would expand the paper significantly.

Response: A section on lymph nodes has been added on pages 15 and 16 of the manuscript, highlighted in yellow. As the reviewer acknowledges a thorough discussion of this topic would lengthen the paper significantly. The topic is briefly discussed and a large recent meta-analysis and systematic review on the topic of lymph node retrieval methods is referenced.


REVIEWER 00037998

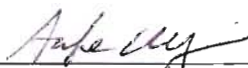
Comment 1: Some minor concerns: Some abbreviations such as TNM, AJCC, RCPATH should be defined in the articles where they first appeared.

Response: These abbreviations are now defined when they first appear on pages 2 and 3, highlighted in yellow.

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

Yours sincerely,


Kieran Sheahan, MB, FRCPI, FRCPath
Clinical Professor, University College Dublin
Consultant Histopathologist


Aoife Maguire, MB, MRCPI, FRCPath
Histopathology SpR