



June 9, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: ESPS Manuscript 10737 - edited_plain text.doc).

Title: Bovine Immunoglobulin Protein Isolates for the Nutritional Management of Enteropathy

Authors: Bryon W. Petschow, Anthony T. Blikslager, Eric M. Weaver, Joy M. Campbell, Javier Polo, Audrey L. Shaw, Bruce P. Burnett, Gerald L. Klein, J. Marc Rhoads

Name of Journal: *World Journal of Gastroenterology*

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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

(1) **Reviewer code:** 01434943 – the abstract states that several different types of enteropathy exist. Additional text has been added to the Introduction (p. 5) to expand on the types of enteropathies and the various therapies that are available (p. 6). Reviewer also suggests adding discussion of hyperimmune colostrums vaccines. The authors acknowledge this is a relevant area but feel strongly that a review of hyperimmune colostrums merits a separate review simply due to the sheer volume of literature on the topic and is beyond the scope of this review of natural immunoglobulin concentrates from plasma or serum. Similarly, the authors feel discussion of IgA concentrations in equine serum or milk is beyond the scope of this review.

(2) **Reviewer code:** 01298827 – Authors agree that radiation enteropathy should be mentioned. Both the Abstract and Introduction have been modified to include mention of radiation enteropathy and the recommended reference has been cited in the Introduction.

(3) **Reviewer code:** 00034179 – Authors agree that the manuscript would benefit from more detailed discussion of cell types and mediators involved in the mechanism of action for SBI. Much of the section detailing the mechanism of action on pages 18-19 have been rewritten to expand on the potential role for SBI in modulating the immune response by binding microbiota components and thereby preventing signaling by toll-like receptors (TLRs) on macrophages, dendritic cells, and epithelial cells. A figure has also been added (Figure 3) which describes how SBI may interact with immune cells present in the gut mucosa to down regulate intestinal inflammation.

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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