

April 5th, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 2123-review.doc).

**Title:** Diagnostic accuracy of a new point-of-care screening assay for celiac disease.

**Authors :** Faiza Benkebil, Christophe Combescure, Silvia I Anghel, Cécile Besson Duvanel, Michela G Schäppi

**Name of Journal :** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 2123

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

**1.Paper was reformatted according to BPG policies for brief article and typos were corrected**

**2.Editor:**

- AmEditor has gone over the entire paper and made the appropriate modifications to the revised text. Language certificate letter from AmEditor is provided.
- Copyright assignment was signed
- p-values & relevant data: According to Editor request, relevant data was provided in the Result section from the Abstract. The use of ROC curve is largely accepted to evaluate diagnostic tools performance. A ROC curve is more informative than a simple comparison of means between cases and controls. The 95% intervals around the AUCs (sensitivities, specificities, likelihood ratios) were systematically reported to show the precision in the estimates.

- Results were reformatted and subheadings were added
- Discussion was updated

### **3. Reviewer 01293353:**

*This is a nice study to examine the accuracy of newly designed CD-LFIA test, and the results are interesting. It is better to give a clear description of the patients who have been received the tests, and present their basic characteristics. DQ2 and DQ8 genes were examined in this study, as shown in the method section, but nothing showed in result section. and what is the aim of study of these genes?*

Unfortunately the HLA typing on DQ2 and DQ8 was only performed on 18 patients of the 112 patients included in the present study, making difficult any statistical analysis. Therefore, we have decided to withdraw these results from the manuscript.

### **4. Reviewer 02441247:**

*Similar paper has been published in E.J. of Gastroenterology and Hepatology with very similar results and conclusions i.e. deamidated gliadin peptides are very useful in point-of-care test diagnosis. It seems that both papers has been solicited from the same company (Augurix SA. This does not necessarily means that papaer should not been published.*

Indeed, the accuracy of the CD-LFIA test was previously study in a pediatric population (mean age of 8.3 years) by Bienvenu et al, 2012. In the present study, the accuracy of CD-LFIA was studied on a mixed pediatric and adult population (mean of age 24.6 years).

### **5. Reviewer 00159281:**

*This is an interesting paper but the following comments should be revising: Abstract: 1-The length of this section is irregular and did not follow the journal instruction.*

- The authors strictly followed BPG requirements concerning the length of the abstract. In the hope of answering to Reviewer concern, the Abstract was slightly reformatted.

*2- In method section please clearly mention the DGP & 3- Also in this section the authors did not mention any info regarding the IgG and IgA.*

- We agree with Reviewer, DGP was not mentioned in the Method section from the Abstract. Therefore, IgA and IgG against DGP is clearly stated in the new version.

*Introduction: 1- Page 6 last paragraph: don't need mention the company name everywhere in the paper. Just mention it in the method section.*

- As suggested by Reviewer, the name of the company was withdrawal from the Introduction.

*Result: 1- Please talk more regarding HLA typing in the study population.*

- For answer regarding HLA DQ2 and DQ8 typing, please refer to answer to Reviewer 01293353.

*2- The tables are some confusing and the authors may match these two tables and present one suitable table.*

- In the hope of clarifying the tables, the legends were slightly modified.

*Discussion: 1- The authors did not show any result regarding these 8 new CD were typical or atypical to compare the sensitivity and specificity of new test.*

- Information on the eight CD new cases was introduced in the Results section

2- *In my opinion one of the big problems of this test is that we cannot distinguish IgA from IgG positive and therefore these false positive/negative may resulted from this.*

- CD-LFIA test measures simultaneously IgA and IgG DGP as well as the total IgA. We believe that this is a rather convenient way of ruling out CD by one simpler test in IgA competent and IgA- deficient patients. Moreover, the false negative results that we have obtained concerned patients on a gluten free diet. This represents a category of patients very difficult to follow because their antibody titers are often around cut-off, depending on the antibody initial levels, time since GFD introduction and compliance to diet. Our four false negative results had IgA-tTG levels near cut-off (36 to 55 U/ml) and a Rann intensity score of 0 on the CD-LFIA test (no band).

3- *As the sample size was very low we cannot suggest this new test in screening of a large scale high-risk population.*

- Large-scale high-risk population was withdrawn from the manuscript

3- *The authors should discuss the following sentence: As the result showed this test is suitable only for diagnosis new celiac cases.*

- We believe that the CD-LFIA test is an accurate test on ruling out CD (sensitivity of 100%, LR- close to 0). The particular challenges to this test is the interpretation of samples with weak reactivity as observed when monitoring GFD. For this specific group, another approach may be required.

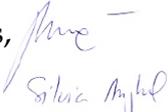
#### **6. Reviewer 00050564:**

*following similar research paper has already been published - Franc? oise Bienvenua, Ce' cile Besson Duvanelc, Camille Seignoverta, Paul Rouzairia, Alain Lachauxb and Jacques Bienvenua. Evaluation of a point-of-care test based on deamidated gliadin peptides for celiac disease screening in a large pediatric population. European Journal of Gastroenterology & Hepatology ,2012*

- For answer, please refer to answer to Reviewer 02441247.

We would like to thank the Editor and Reviewers for their constructive feedbacks.

Thank you of considering our manuscript for publication in the *World Journal of Gastroenterology*.

Sincerely yours, 

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