REVIEWER 1: I reviewed the above mentioned manuscript from Rodriguez et al. evaluating the correlation of the Rapid Point-of-Care fecal calprotectin test versus an ELISA test for pediatric IBD patients. To reach this aim they analysed 49 stool samples of 31 pediatric IBD patients with both methods. This is a prospective trial studying the correlation of POC versus ELISA in pediatric IBD. The authors pointed out the following finding: - There is a better correlation between POC and ELISA in the lower range (<250µg/g) and less correlation at higher calprotectin levels. However, the major key point of criticism of this manuscript is, that their finding has already be shown with the same calprotectin POC test (Quantum Blue? Extended immunoassay (Bühlmann Laboratories, Switzerland)) in the publication of Kolho et al 2012. Kolho analysed 134 stool samples of 56 patients at time of diagnosis and during induction therapy. They also show a better correlation for values below 300µg/g calprotectin. The Quantum Blue ? Test was already evaluated for the usage in IBD patients (Wassel et al 2012). In addition, Inoue et al. described another calprotectin rapid assay system in 131 pediatric UC, 121 pediatric CD patients, and 57 controls and correlated this results with the endoscopic score. Thus this study does not provide any new information and was performed with a limited sample size. No other correlations regarding PCDAI or endoscopic score are provided, no healthy controls were analysed. Minor essential revision: The statement that calprotectin levels below <250µg/g correlate with quiescence is not correct.

AUTHORS' RESPONSE: We acknowledge the limitations to our study. Other than the Inoue et al study, our study would be the second to show correlation between the point-of-care assay and the send-out ELISA calprotectin test. Also, we are the first group to report on such correlation in the United States. Monitoring calprotectin levels is not standard of care in the U.S., and the practice is much more adopted in Europe. There is only one FDA approved calprotectin assay; the Quantum Blue is not approved in the U.S.

Considering pediatric IBD patients in the U.S. using this research-only point of care assay, we believe the study is worth reporting. Furthermore, we have used a very methodologically sound statistical method that has not been reported. Arguably, our Bland Altman plot is superior in how a correlation study should be reported when comparing two diagnostic tests. As the reviewer has suggested, we have edited the statement that calprotectin levels below <250µg/g correlate with quiescence.

REVIEWER 2: General comment: This is a well done prospective study about the comparison of two types of fecal calprotectin diagnostic methods as possible markers for assessment the pediatric IBD disease severity. Major comments: - the number of included patients and samples is small. There should be a paragraph about the study limitations at the end of the manuscript. - in the discussion part the authors should compare their data more extensively with the data of previous studies in adults and also in children (e.g. Kolho et al, JPGN 2012). - the description of patients is not sufficient. The Table 1 should be extended with more data like for example: PUCAI and PCDAI numbers… - it should be clearly stated if stool samples were properly collected as for example that it were not collected during colon cleansing procedure.

AUTHORS' RESPONSE: Thank you for your positive review. We have clarified the limitation of the small sample size as the reviewer suggested. We have added more descriptive discussion between our study and Kolho et al. With regards to adding PUCAI and PCDAI, since this study performed in various clinical settings (e.g., an infusion unit), disease indices were not tracked as they would be if all patient encounters were from an outpatient clinic. We have added a statement how the samples were collected appropriately (i.e., not during colon cleansing).

REVIEWER 3: The authors in their study compared two calprotectin tests, send-out ELISA test and point-of-care (POC) test in pediatric IBD patients. They

prospectively enrolled 31 pediatric IBD and collected 49 stool samples for assessment. The authors concluded that there is better correlation between these two tests at low-range levels of calprotectin, < 250ug/g. This is important conclusion regarding non-invasive method of IBD activity assessment, which is essential at the onset of disease and during relapses. Actually, only a few papers were published up to now within this field. Major comments: 1.This is interesting observation but performed on very small group of patients; (in FC < 250 ug/g: CD – 9, UC – 10, IBD-U – 2 patients). There is also very limited data regarding characteristics of IBD group. What was clinical presentation at the time of assessment? What was the clinical activity of IBD at the time of assessment (PCDAI, PUCAI)? What was the location and severity of the inflammatory lesions? What treatment was used in IBD patients? 2.Additionally, some patients were tested twice or more. What was the indication for repeated calprotectin assessment? What correlation was found within this subgroup? 3.What kind of stools were collected from IBD children using the CALEX cap devise, eg. solid, semi-liquid, liquid or water-like ones? Because, by using this method of stool samples collection, the kind of stool may influence the results, secondary to different amount of stool which is adhered to the stick. This data should be presented and discussed by the authors Minor points: Some similar studies were published up to now, in IBD children and adults. The authors should discuss and compare their own results with these data in more detailed manner [e.g. Kolho KL et al. JPGN 2012; 55: 436-439; Labaere D et al. UEG Journal 2014; 2: 30-37, Delefortrie Q et al. Clin Biochem 2016; 49: 268-273]

AUTHORS' RESPONSE: Thank you for your positive review, and we agree that supporting the evidence that calprotectin levels <250 are RELIABLE whether clinicians use the point-of-care test or the send-out ELISA is an important finding. The majority of these patients were approached / recruited in an outpatient infusion center (when they were there for their infliximab infusion, not in clinic. Therefore, since their clinician is

not seeing them and generating a note, it is not possible to generate more longitudinal patient-specific attributes. This was not the goal for this project since we really just wanted to answer the question of the strength of correlation between two calprotectin tests. We added more discussion comparing our study with other studies.