Key Literature – BÜHLMANN fecal Calprotectin Citations

A number of the publications in the citation list describe applications that are outside of FAA cleared product claims thus they should be used for information only.

BÜHLMANN fCAL® ELISA is FDA 510(k) cleared. For in vitro Diagnostic Use. (Intended Use: The BÜHLMANN fCAL® ELISA aids in the diagnosis of inflammatory bowel disease (IBD), specifically Crohn’s disease (CD) and ulcerative colitis (UC) and aids in the differentiation of IBD from irritable bowel syndrome (IBS) in conjunction with other laboratory and clinical findings.)

BÜHLMANN fCAL® turbo and Quantum Blue® fCAL Assays are for Research Use Only. Not for use in diagnostic procedures in the US.

Value of fecal Calprotectin in IBD:

- Jensen, M.D. et al., 2011, Fecal calprotectin is equally sensitive in Crohn’s disease affecting the small bowel and colon, Scandinavian Journal of Gastroenterology
  “The first study to show that fecal calprotectin is equally sensitive in colonic and small bowel CD.”

- Mindemark, M. & Larsson, A. 2012, Ruling out IBD: Estimation of the possible economic effects of pre-endoscopic screening with F-calprotectin, Clinical Biochemistry
  “The estimated demand for colonoscopies was reduced by 50% to 67%. This corresponded to a cost avoidance of approximately up to €2.13 million.”

Diagnosis of IBD patients:

- Burri, E. et al., 2013, Monoclonal antibody testing for fecal calprotectin is superior to polyclonal testing of fecal calprotectin and lactoferrin to identify organic intestinal disease in patients with abdominal discomfort, Clinica Chimica Acta
  “...we demonstrated, that the diagnostic accuracy of monoclonal antibody testing of calprotectin is superior to both polyclonal antibody testing...”

  “Bühlmann assays were superior with 100% sensitivity...”

- Labaere, D. et al., 2014, Comparison of six different calprotectin assays for the assessment of inflammatory bowel disease, United European Gastroenterology Journal
  “The ELA [Phadia] cut off for diagnosis was optimal at a level of 15 mg/g. This is as low as the detection limit of the assay, which is analytically unacceptable.”

- Manz, M. et al., 2012, Value of fecal calprotectin in the evaluation of patients with abdominal discomfort: an observational study, BMC Gastroenterology
  “All together, those results support the concept that fecal calprotectin is a useful marker in the evaluation of patients with abdominal discomfort...”

- Sydora, M. J. et al., 2012, Validation of a point-of-care desktop device to quantitate fecal calprotectin and distinguish inflammatory bowel disease from irritable bowel syndrome, Journal of Crohn’s and Colitis
  “Quantum Blue Reader® calprotectin levels were available within 30 min and correlated well with results derived from standard ELISA assays.”

Other Applications for IBD Patients:

- Abej, E. et al., 2016, The Utility of Fecal Calprotectin in the Real-World Clinical Care of Patients with Inflammatory Bowel Disease, Canadian Journal of Gastroenterology and Hepatology
  “…positive FCAL was significantly associated with abnormal endoscopy, elevated serum CRP, low serum Hg, and low serum albumin.”

- Coorevits, L. et al., 2012, Faecal calprotectin: comparative study of the Quantum Blue rapid test and an established ELISA method, Clinical Chemistry and Laboratory Medicine: CCLM / FESCC
  “…we may conclude that the POCT can serve as reliable alternative to the time consuming ELISA...”

- Ferreiro-Iglesias, R. et al., 2016, Accuracy of Consecutive Fecal Calprotectin Measurements to Predict Relapse in Inflammatory Bowel Disease Patients Under Maintenance With Anti-TNF Therapy, J Clin Gastroenterol
  “…time interval to the next FC measurement should be probably shorter than 4 months after a FC result of 130 to 300 mg/g...”
• Ferreiro-Iglesias, R. et al., 2015, Fecal Calprotectin as Predictor of Relapse in Patients With Inflammatory Bowel Disease Under Maintenance Infliximab Therapy, *J Clin Gastroenterol*
  “We found FC to be a very accurate marker to exclude relapse within the following 2 month after administration of Infliximab.”

• Guardiola, J. et al., 2014, Fecal Level of Calprotectin Identifies Histologic Inflammation in Patients with Ulcerative Colitis In Clinical And Endoscopic Remission, *Clinical Gastroenterology and Hepatology*
  “...an FC value less than 155 mg/g is a reliable indicator of the absence of acute inflammatory infiltrate (negative predictive value, 89%).”

• Kostas, A. et al., 2017, Fecal calprotectin measurement is a marker of short-term clinical outcome and presence of mucosal healing in patients with inflammatory bowel disease, *World J Gastroenterol*
  “...In our patient cohort, we were able to define an optimal cut-off FC value of 261 mg/g, which had a strong predictive value for the discrimination of future relapses vs maintenance of remission.”

• Lasson, A. et al., 2014, Pharmacological intervention based on fecal calprotectin levels in patients with ulcerative colitis at high risk of relapse: A prospective, randomized, controlled study, *United European Gastroenterology Journal*
  “In patients with UC, FC-guided dosing of the patient’s 5-ASA agent showed significantly lower relapse rates than for patients in the control group.”

• Lobatón, T. et al., 2013, A new rapid test for fecal calprotectin predicts endoscopic remission and postoperative recurrence in Crohn’s disease, *Journal of Crohn’s & Colitis*
  “FC determined by rapid quantitative test predicts “endoscopic remission” and endoscopic postoperative recurrence in CD patients.”

• Lobatón Ortega, T. et al., 2013, A New Rapid Quantitative Test for fecal Calprotectin Predicts Endoscopic Activity in Ulcerative Colitis, *Inflammatory bowel diseases*
  “FC determined by QPOCT was an accurate surrogate marker of “endoscopic remission” in UC presented a good correlation with the FC-ELISA test.”

• Louis Edouard, 2015, Fecal calprotectin: towards a standardized use for inflammatory bowel disease management in routine practice, *Journal of Crohn’s and Colitis*
  “...fecal calprotectin as a unique first line test would be sufficient to decide in which patient to perform further endoscopic or medical imaging explorations.”

• Magro, F. et al., 2018, Comparison of different histological indexes in the assessment of UC activity and their accuracy regarding endoscopic outcomes and faecal calprotectin levels, *Inflamm bowel dis*
  “…81 %, 93 % and 85 % of the patients that have an FC level below 150µg/g (using the QB method) are in histological remission according to NI, RHI and GS (using 3.1 as the cut-off).”

• Naismith, G. D. et al., 2014, A prospective evaluation of the predictive value of faecal calprotectin in quiescent Crohn’s disease, *Journal of Crohn’s and Colitis*
  “The FC result, obtained by non-invasive means, can provide prognostic information for both the patient and clinician alike.”

• Nakov, R. V. et al., 2018, Fecal Calprotectin for Assessment of Inflammatory Bowel Disease Activity, *Clin Res Immunology*
  “The ROC analysis found that a cutoff FCP level of 315 µg/g differentiates quiescent CD from active ileal disease with 94% sensitivity, 98% specificity, and area under the curve (AUC) 0.984.”

• Pavlidis, P. et al., 2016, Early change in faecal calprotectin predicts primary non-response to anti-TNFα therapy in Crohn’s disease, *Scandinavian Journal of Gastroenterology*
  “The AFCAL could act as an ‘early warning’ to consider alternatives such as dose optimisation or another biologic with a different mode of action, rather than persisting for several months.”

• Roblin, X. et al., 2017, Development and Internal Validation of a Model Using Fecal Calprotectin in Combination with Infliximab Trough Levels to Predict Clinical Relapse in Crohn’s Disease, *Inflamm Bowel Dis*
  “In IFX-treated patients with CD in clinical remission, a combination of TLI (<2 µg/mL) and fecal calprotectin (>250 µg/g of stools) is a good model for predicting loss of response.”

• Rosenfeld, G. et al., 2016, Focus: Future of fecal calprotectin utility in inflammatory bowel disease, *World J Gastroenterol*
  “...FC is a simple, non-invasive test that is gaining widespread use in the diagnosis and management of IBD.”

• Theede, K. et al., 2016, Fecal Calprotectin Predicts Relapse and Histological Mucosal Healing in Ulcerative Colitis, *Inflamm Bowel Dis*
  “Two consecutive measurements of a 1-month interval with FC >300 mg/kg were most predictive of relapse.”
• Turvill, J. et al., 2017, Validation of a care pathway for use of faecal calprotectin in monitoring patients with Crohn’s disease, *Frontline Gastroenterology*
  
  “…the PPV of 0.85 and a NPV of 0.97 of this clinical validation are compelling…”

• Voiosu, T. et al., 2014, Rapid Fecal Calprotectin Level Assessment and the SIBDQ Score Can Accurately Detect Active Mucosal Inflammation in IBD Patients in Clinical Remission: a Prospective Study, *J Gastrointestin Liver Dis*
  
  “FC levels appears to be a practical method for monitoring disease activity in these patients, possibly reducing the need for repeat endoscopic examinations.”

• Wright, E. K. et al., 2016, Comparison of Fecal Inflammatory Markers in Crohn’s Disease, *Inflamm Bowel Dis*
  
  “This study shows that FC is the optimal marker for diagnosing and monitoring endoscopic postoperative recurrence.”

• Wright, E. K. et al., 2015, Measurement of Fecal Calprotectin Improves Monitoring and Detection of Recurrence of Crohn’s Disease After Surgery, *Gastroenterology*
  
  “The present study has shown that FC concentration is sufficiently sensitive to monitor for recurrence of Crohn’s disease.”

• Zhulina, Y. et al., 2016, The prognostic significance of faecal calprotectin in patients with inactive inflammatory bowel disease, *Aliment Pharmacol Ther*
  
  “Our data suggest that longitudinal monitoring of faecal calprotectin is informative in predicting relapse in IBD.”

Special Focus on Cut-off:

• Pavlidis, P. et al., 2013, Diagnostic accuracy and clinical application of faecal calprotectin in adult patients presenting with gastrointestinal symptoms in primary care, *Scandinavian Journal of Gastroenterology*
  
  “This study provides the first evidence on the use of fCal (BÜHLMANN fCAL® ELISA) testing in primary care…..to be used as part of the pathway for management of patients with suspected IBS.”

• Seenan, J.P. et al., 2015, Are we exposing patients with a mildly elevated faecal calprotectin to unnecessary investigations?, *Gastroenterology*
  
  “we propose an alternative diagnostic approach of repeating the FC after 6-8 weeks in patients with values of 100-200 µg/g.”

• Walsham and Sherwood, 2016, Fecal calprotectin in inflammatory bowel disease, *Clinical and Experimental Gastroenterology*
  
  “The choice of a cutoff will depend on whether sensitivity or specificity is considered to be the most important and needs to be made taking into consideration the clinical features of an individual patient.”

The use of fecal Calprotectin in Pediatrics:

  
  “The area under the curve (AUC) for discrimination between subgroup of patients in remission vs moderate disease was 0.90 with cut-off level of 300 µg/g and sensitivity 0.89, specificity 0.82.”

• Prell, C. et al., 2014, Comparison of three tests for faecal calprotectin in children and young adults: a retrospective monocentric study, *BMJ Open*
  
  “In conclusion, measurement of FC in paediatric patients with unspecific symptoms is very helpful in order to avoid invasive procedure.”

  
  “…we present the first correlation study of rapid POC calprotectin testing in a pediatric IBD cohort in the United States.”

• Zhu, Q. et al., 2016, Fecal Calprotectin in Healthy Children Aged 1-4 Years, *PLOS ONE*
  
  “Children aged from 1 to 4 years old have lower FC concentrations compared with healthy infants (<1 years), and higher FC concentrations when comparing with children older than 4 years and adults.”
Further Literature citing the BÜHLMANN fecal Calprotectin Assays:

- Brandse, J.F. et al., 2016, Performance of Common Disease Activity Markers as a Reflection of Inflammatory Burden in Ulcerative Colitis, *Inflamm Bowel Dis*
- Burri, E. et al., 2014, Diagnostic yield of endoscopy in patients with abdominal complaints: incremental value of faecal calprotectin on guidelines of appropriateness, *BMC Gastroenterology*
- Calafat, M. et al., 2015, High Within-day Variability of Fecal Calprotectin Levels in Patients with Active Ulcerative Colitis: What Is the Best Timing for Stool Sampling? *Inflamm Bowel Dis*
- Chang, M. et al., 2014, Faecal calprotectin as a novel biomarker for differentiating between inflammatory bowel disease and irritable bowel syndrome, *Molecular Medicine Reports*
- Delefortrie, Q. et al., 2015, Comparison of the Liaison® Calprotectin kit with a well-established point of care test (Quantum Blue — Bühlmann-Alere®) in terms of analytical performances and ability to detect relapses amongst a Crohn population in follow-up, *Clinical Biochemistry*
- Dhaliwal, A. et al., 2014, Utility of faecal calprotectin in inflammatory bowel disease (IBD): what cut-offs should we apply? *Frontline Gastroenterology*
- Du, L. et al., 2016, Within-Stool and Within-Day Sample Variability of Fecal Calprotectin in Patients With Inflammatory Bowel Disease, *J Clin Gastroenteral*
- Ferreiro-Iglesias, R. et al., 2015, Usefulness of a rapid faecal calprotectin test to predict relapse in Crohn’s disease patients on maintenance treatment with adalimumab, *Scandinavian Journal of Gastroenterology*
- Frin, A-C. et al., 2016, Accuracies of fecal calprotectin, lactoferrin, M2-pyruvate kinase, neopterin and zonulin to predict the response to infliximab in ulcerative colitis, *Digestive and Liver Disease*
- Gaus, A. et al., 2016, Quality of Life Is Related to Fecal Calprotectin Concentrations in Colonic Crohn Disease and Ulcerative Colitis, but not in Ileal Crohn Disease, *Medicine*
- Halfvarson, J. et al., 2017, Dynamics of the human gut microbiome in inflammatory bowel disease, *Nature Microbiology*
- Kok, L. et al., 2012, Diagnostic Accuracy of Point-of-Care Fecal Calprotectin and Immunochemical Occult Blood Tests for Diagnosis of Organic Bowel Disease in Primary Care: The Cost-Effectiveness of a Decision Rule for Abdominal Complaints in Primary Care (CEDAR) Study, *Clinical Chemistry*
- Kolho, K. et al., 2012, Rapid Test for Fecal Calprotectin Levels in Children With Crohn Disease, *JPGN*
- Kristensen, V. et al., 2015, Prediction of Endoscopic Disease Activity in Ulcerative Colitis by Two Different Assays for Fecal Calprotectin, *Journal of Crohn’s and Colitis*
- Lasson, A. et al., 2015, The Intra-Individual Variability of Faecal Calprotectin: A Prospective Study In Patients With Active Ulcerative Colitis, *Journal of Crohn’s and Colitis*
- Levine, A. et al., 2014, Comparison of Outcomes Parameters for Induction of Remission in New Onset Pediatric Crohn’s Disease: Evaluation of the Porto IBD Group “Growth Relapse and Outcomes with Therapy”, *Inflamm Bowel Dis*
- Li, F. et al., 2014, Comparison of the different kinds of feeding on the level of fecal calprotectin, *Early Human Development*
- Lin, Wei-Chen et al., 2015, Fecal calprotectin correlated with endoscopic remission for Asian inflammatory bowel disease patients, *World J Gastroenteral*
- Noebauer, B. et al., 2017, Analytical evaluation of a fully automated immunoassay for faecal calprotectin in a paediatric setting, *Biochem Med (Zagreb)*
- Oyaert, M. et al., 2013, Comparison of two immunoassays for measurement of faecal calprotectin in detection of inflammatory bowel disease: (pre)-analytical and diagnostic performance characteristics, *Clin Chem Lab Med*
- Paul, S. et al., 2013, Therapeutic Drug Monitoring of Infliximab and Mucosal Healing in Inflammatory Bowel Disease: A Prospective Study, *Inflamm Bowel Dis*
- Rogler, G. et al., 2013, Concept for a rapid point-of-care calprotectin diagnostic test for diagnosis and disease activity monitoring in patients with inflammatory bowel disease: Expert clinical opinion, *Journal of Crohn’s and Colitis*
- Wang, S. et al., 2014, Faecal calprotectin concentrations in gastrointestinal diseases, *Journal of International Medical Research*