



**CALPROTECTIN**

**EliA™**  
*Excellence in Autoimmunity*

# Identify inflammatory bowel diseases **clearly and efficiently**

EliA™ Calprotectin – the first fully automated calprotectin stool test

**Thermo**  
SCIENTIFIC

## Is it inflammatory?

### **EliA™ Calprotectin – providing early diagnostic guidance in a fast, cost efficient manner**

Fecal calprotectin is a very sensitive and specific marker for inflammation in the intestinal tract: as a first line test, a negative result can rule out an inflammatory process while a positive result may prioritize endoscopy in the diagnostic path.<sup>4</sup>

Fecal calprotectin is an efficient marker for therapeutic effectiveness and mucosal healing since its level correlates well with endoscopic and histological findings in inflammatory bowel diseases.<sup>2,7</sup> In recent studies it was possible to predict relapse in Crohn's disease and ulcerative colitis.<sup>6,8,9</sup>

**Fecal calprotectin can now be measured with a fast, fully automated test leading to improved operational efficiency and minimized costs: EliA™ Calprotectin.**

# EliA™ Calprotectin – clear IBD/IBS differentiation

## Excellent performance, high predictive values

The outstanding performance of EliA™ Calprotectin is underlined by the high sensitivity and the high specificity of the test (Table 1). Most important, the predictive values and the likelihood ratios give excellent values assuring **high clinical usefulness of the test in routine practice**.

High clinical value	EliA™	Supplier 1	Supplier 2
Sensitivity	97.7 %	96.7 %	99.2 %
Specificity	89.8 %	89.8 %	76.3 %
Positive predictive value (PPV)	0.96	0.96	0.90
Negative predictive value (NPV)	0.95	0.93	0.98
Positive likelihood ratio (LR+)*	9.58	9.48	4.19
Negative likelihood ratio (LR-)*	0.03	0.04	0.01

Table 1: Performance data of EliA™ Calprotectin and tests from two other suppliers (internal study)



## Identifies IBD clearly

An internal **clinical study** showed that EliA™ Calprotectin is able to differentiate clearly between inflammatory bowel diseases (IBD), irritable bowel syndrome (IBS) and other functional bowel disorders (BD) (Figure 1).

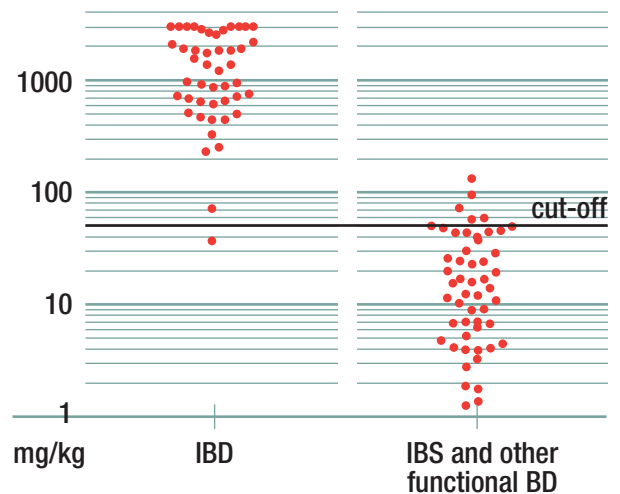


Figure 1: Performance of EliA™ Calprotectin in 191 clinically defined patients – 132 IBD, 59 IBS, and other functional bowel disorders (BD). A value of 50 mg/kg is set as cut-off for positivity. (internal study)

## EliA™ Calprotectin – fast, fully automated testing

Routine stool extraction samples are processed automatically by the Phadia® Laboratory Systems by reducing the workload for the lab personnel. The four available instruments – Phadia® 100, Phadia® 250, Phadia® 2500 and Phadia® 5000 – are designed to meet the specific needs of the laboratory. EliA™ Calprotectin can easily be performed together with EliA™ serum tests for celiac disease or food allergy, even simultaneously. **This provides flexibility, saves costs, and assures a quick delivery of results for improved service quality.**

### \* Likelihood Ratios – diagnostic evidence or not

Likelihood ratios use the sensitivity and specificity of a test to determine if the positive or negative result of a diagnostic test changes the probability of the patient actually being afflicted with the disease.

LR+ = Sensitivity / (1-Specificity)

LR- = (1-Sensitivity) / Specificity

Diagnostic evidence:

LR+ 0 - 2 none

LR+ 2 - 5 weak

LR+ 5 - 10 moderate

LR+ > 10 high

LR- > 0.5 none

LR- 0.2 - 0.5 weak

LR- 0.1 - 0.2 moderate

LR- < 0.1 high

The high LR+ value of calprotectin measurement shows the conclusive power of a positive test result for inflammation in the intestine.

# Fecal calprotectin – a precise marker for intestinal inflammation: non-invasive, specific, and sensitive

Inflammation is characterized by an increased activity of immune cells (e.g. neutrophil granulocytes) which release pathogen attacking substances such as calprotectin. In intestinal inflammation the barrier function of the intestinal wall is lost and neutrophil granulocytes migrate through the wall into the intestinal lumen. This leads to an elevated calprotectin level in the stool.<sup>3</sup> The level of fecal calprotectin correlates directly to the number of neutrophil granulocytes in the intestinal lumen. As such it is specifically elevated in inflammatory bowel diseases (IBD) such as Crohn's disease and ulcerative colitis and to a much smaller extent in other entities such as neoplasia and polyps. This correlation also makes stool calprotectin a very specific and sensitive marker in indicating intestinal inflammation.<sup>3</sup> **The level of calprotectin in feces is approximately 6 times higher than in serum. This makes stool testing more sensitive in addition to its higher specificity for intestinal diseases.<sup>4</sup>**

## Recommended as a first line test

Together with CRP, ESR, and stool culture, the measurement of stool calprotectin is useful as a screening test in all subjects reporting gastrointestinal (GI) problems.<sup>4</sup> Since complaints such as abdominal pain, diarrhea, and bloating are very frequent and are common to several GI diseases which would require different therapeutic approaches, it is crucial to discriminate between inflammatory and non-inflammatory disorders; i.e. between inflammatory bowel diseases (IBD) and non-inflammatory diseases, such as irritable bowel syndrome (IBS). **A negative calprotectin result in a patient without alarm symptoms is reason enough to avoid endoscopy** while a positive result can prioritize invasive and expensive procedures such as endoscopy including intestinal biopsy. The measurement of calprotectin provides an important orientation for the physician in the diagnosis of GI patients.

## Non-invasive testing with high clinical value

Stool calprotectin measurement is an easy, non-invasive first line test which clearly differentiates IBD from IBS and other functional disorders. It has been shown to be the most sensitive and most specific test for this discrimination **clearly outperforming blood tests such as CRP or ESR** (Figure 2).<sup>5</sup> The high positive and negative predictive value of fecal calprotectin provides valuable help in the diagnostic process.<sup>5</sup> Furthermore, stool calprotectin correlates with disease activity and allows the prediction of relapses in IBD.<sup>6</sup> This makes calprotectin useful for both the diagnosis and the monitoring of IBD patients.

Figure 2, 3: Crohn's disease and ulcerative colitis (UC)

**Location of inflammatory changes: Crohn's disease can affect any part of the gastrointestinal tract, from mouth to anus (skip lesions). The majority of cases start in the terminal ileum. UC is restricted to the colon and the rectum.**

### Crohn's disease

Skip lesions

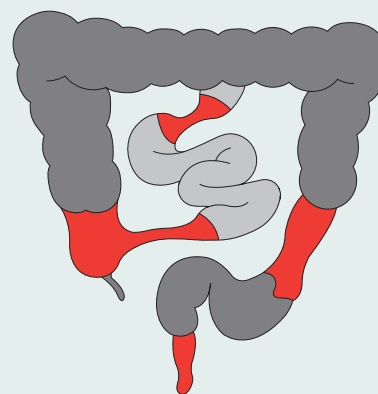


Figure 2

### Definition of fecal calprotectin

Calprotectin is an abundant protein in pathogen defense. The calcium- and zinc-binding protein is predominantly present in the cytoplasm of cells involved in pathogen defense such as neutrophil granulocytes, monocytes, and macrophages. Calprotectin shows bacteriostatic and fungistatic properties in vitro which underline its function in pathogen attack. In neutrophil granulocytes it accounts for as much as 60% of the cytosolic protein.<sup>1,2</sup>

### Ulcerative colitis

Continuous colonic involvement beginning in rectum

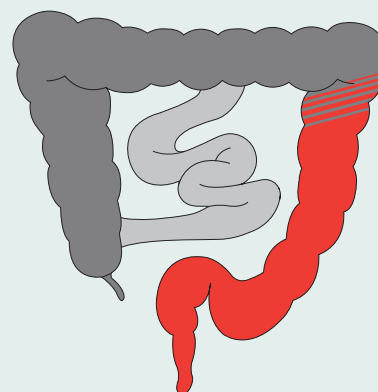


Figure 3

# Crohn's disease/IBS – fecal calprotectin minimizes false positives

## Fecal Calprotectin is more effective

Fecal calprotectin is more effective in terms of diagnostic accuracy than the standard tests ESR and CPR currently used for distinguishing IBD from IBS.<sup>10</sup> **Fecal calprotectin minimizes the number of false positive results and reduces the number of unnecessary biopsies.**

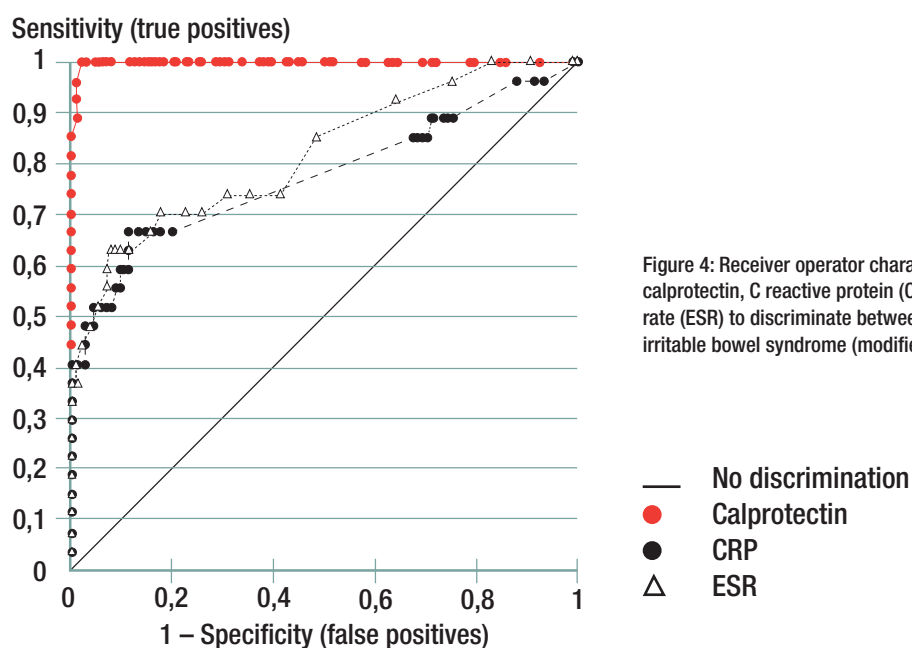


Figure 4: Receiver operator characteristic analysis of the ability of calprotectin, C reactive protein (CRP), and erythrocyte sedimentation rate (ESR) to discriminate between patients with Crohn's disease and irritable bowel syndrome (modified after Tibble et al 2000).<sup>8</sup>

## Your Advantages with EliA™ Calprotectin:

- clear differentiation between IBD and IBS
- early diagnostic guidance
- completely automated and efficient testing
- reducing the workload for your lab personnel
- add-on to the EliA™ gastro panel on Phadia® Laboratory Systems

### References:

1 Gaya DR, Mackenzie JF (2002). *Faecal calprotectin: a bright future for assessing disease activity in Crohn's disease.* *Q J Med* 95: 557-558 2 Roseth AG et al (2004). *Normalization of faecal calprotectin: a predictor of mucosal healing in patients with inflammatory bowel disease.* *Scand J Gastroenterol* 39: 1017-1020 3 Vermeire S et al (2006). *Laboratory markers in IBD: useful, magic or unnecessary toys?* *Gut* 55: 426-431 4 Summerton CB et al (2002). *Faecal calprotectin: a marker of inflammation throughout the intestinal tract.* *Eur J Gastroenterol Hepatol* 14: 841-845 5 Tibble J et al (2000). *A simple method for assessing intestinal inflammation in Crohn's disease.* *Gut* 47: 506-513 6 Sutherland AD et al (2008). *Review of fecal biomarkers in inflammatory bowel disease.* *Dis Colon Rectum* 51: 1283-1291 7 Roseth AG et al (1997). *Assessment of disease activity in ulcerative colitis by faecal calprotectin, a novel granulocyte marker protein.* *Digestion* 58: 176-80 8 Tibble JA et al (2000). *Surrogate markers of intestinal inflammation are predictive of relapse in patients with inflammatory bowel disease.* *Gastroenterology* 119: 15-22 9 D'Inca R et al (2005). *Can Calprotectin predict relapse in inflammatory bowel disease?* *Gastroenterology* 128 (suppl): A307 10 Centre for Evidence-based Purchasing. *Economic report: Value of calprotectin in screening out irritable bowel syndrome.* NHS Purchasing and Supply Agency: London; 2010 CEP09041

## EliA™ Calprotectin: technical data

EliA™ Calprotectin offers a complete solution: from stool extraction to automated sample measurement.

<b>Coating</b>	Mouse monoclonal antibodies to calprotectin		
<b>Dilution</b>	1:100		
<b>Sample material</b>	Human stool		
<b>Standardization</b>	Six point calibration curve; results in mg/kg		
<b>Cut-off / measuring range</b>	negative	positive	measuring range
	≤ 50 mg/kg	> 50 mg/kg	15 – ≥ 3000 mg/kg

<b>Normal distribution</b> (95 % / 99 % percentile)	27.3 mg/kg / 43.6 mg/kg		
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<b>Reproducibility</b>	Intra-run variance*	2.8 - 7.0 %	
	Inter-run variance*	1.9 - 7.3 %	* for details see directions for use

Ordering information	Package size	Article No.
EliA™ Calprotectin Well	4 x 12 wells	14-5610-01
EliA™ Calprotectin Calibrator Well	4 x 12 wells	14-5618-01
EliA™ Calprotectin Extraction Buffer	6 x 24 tests	83-1068-01
Fecal Extraction Device	50 devices	14-5619-01

### Reagents for Phadia® 100

EliA™ Calprotectin Calibrators	6 vials for 1 curve	83-1058-01
EliA™ Calprotectin Curve Control	6 vials for 6 runs	83-1059-01
EliA™ Calprotectin Conjugate	2 x 48 tests	83-1060-01
EliA™ Calprotectin Conjugate	6 x 48 tests	83-1061-01
EliA™ Calprotectin Positive Control 100	6 vials for 12 tests	83-1066-01
EliA™ Calprotectin Negative Control 100	6 vials for 12 tests	83-1067-01

### Reagents for Phadia® 250/2500/5000

EliA™ Calprotectin Calibrator Strips	5 strips for 5 curves	83-1062-01	
EliA™ Calprotectin Curve Control Strips	5 strips for 30 runs	83-1063-01	
EliA™ Calprotectin Conjugate 50	6 x 50 tests	83-1064-01	
EliA™ Calprotectin Conjugate 200	6 x 200 tests	83-1065-01	
EliA™ Calprotectin Positive Control 250	6 vials for 12 tests	83-1083-01	(for Phadia® 250 only)
EliA™ Calprotectin Negative Control 250	6 vials for 12 tests	83-1085-01	(for Phadia® 250 only)
EliA™ Calprotectin Positive Control 2500/5000	6 vials for 12 tests	83-1084-01	(for Phadia® 2500/5000 only)
EliA™ Calprotectin Negative Control 2500/5000	6 vials for 12 tests	83-1086-01	(for Phadia® 2500/5000 only)