



# Irritable Bowel Syndrome or Inflammatory Bowel Disease?

## PreventID® CalDetect

### Rapid Test for the Determination of Calprotectin in faeces\*

**PreventID® CalDetect is a semiquantitative immunochromatographic rapid test for the determination of faecal calprotectin. Calprotectin has been established as a faecal marker of inflammatory bowel diseases (IBD). It allows a differentiation between organic intestinal diseases and functional intestinal diseases and is ideal for monitoring disease activity. Three test lines facilitate the grading of the calprotectin positivity and thus the assessment of individual disease progression**

Calprotectin (MRP 8/14) is a heterodimer of two calcium-binding proteins present in the cytoplasm of neutrophils and expressed by the membranes of monocytes. It constitutes nearly 60% of the soluble cytosol proteins in neutrophils and plays a central role in neutrophil defense. Upon neutrophil activation or endothelial adhesion of monocytes, calprotectin is released and may be detected in serum, body fluids or stool as a potentially useful clinical inflammatory marker.

The acute phase protein resists metabolic degradation and shows a high stability in faeces (stable for one week at room temperature!). Faecal calprotectin levels correlate significantly with histologic and endoscopic assessment of disease activity in ulcerative colitis (UC), as well as with faecal  $\alpha_1$ -antitrypsin levels and faecal excretion of  $^{111}$ indium-labeled white blood cells in patients with CD (Roseth et al. 1992, Tibble et al. 2000). **Calprotectin has been established as a faecal marker of inflammatory bowel diseases (IBD).** It allows a reliable differentiation between organic intestinal diseases (e.g. chronic inflammatory diseases, infectious diseases, polyps, colon cancer) and functional intestinal diseases (e.g. irritable bowel syndrome, IBS).

Faecal calprotectin has several characteristics of an ideal test: simple, non-invasive, and low cost. These features allow for serial monitoring of the disease activity and treatment success, especially in the evaluation of new and empirical drugs. Most recently this test has been able to disclose treatment failure, allowing for these patients to avoid prolonged, useless courses of steroids.

### Prediction of IBD Relapse

Crohn's disease and ulcerative colitis are related conditions characterized by periods of remission marked by episodes of clinical relapse. The clinical implications of predicting which patients with IBD are likely to relapse are considerable. Such knowledge may allow targeted treatment at an earlier stage (with fewer side effects) to avert the relapse, as well as an assessment of new therapeutic strategies for maintaining symptomatic remission (Hodgson 1999). A study has demonstrated the usefulness of faecal calprotectin in predicting relapse of IBD (Tibble et al. 2000). Calprotectin is ideal for monitoring disease activity (e.g. of M. Crohn or after polyp resection) and early detection of the relapse. The differentiation between negative values, slightly increased values and high calprotectin values is important for excluding functional intestinal diseases (e.g. irritable bowel syndrome) and for the diagnosis and monitoring of organic intestinal diseases.

### Indications for the determination of Calprotectin:

- Differentiation between organic intestinal diseases (e.g. IBD) and functional intestinal diseases (IBS)
- Ideal for monitoring disease activity (e.g. of M. Crohn or after polyp resection)
- Ideal for monitoring the early detection of relapse
- Differentiation between organic diarrhoea and functional diarrhoea

## PreventID® CalDetect (KST11005)

The **PreventID® CalDetect** is a semiquantitative immunochromatographic rapid test for the detection of calprotectin in faeces. The detection of calprotectin in faeces allows a differentiation between organic intestinal diseases (e.g. chronic inflammatory diseases, infectious diseases, polyps, colon cancer) and functional intestinal diseases (e.g. irritable bowel syndrome). The determination of calprotectin is also ideal for monitoring disease activity (e.g. of M. Crohn or after polyp resection), early detection of relapse and for therapy monitoring. Using three test lines allows the physician to distinguish between varying degrees of calprotectin positivity.

Calprotectin (MRP 8/14) is a heteromer of two calcium-binding proteins (MRP8 and MRP 14) present in the cytoplasm of neutrophils and expressed by the membranes of monocytes. It constitutes nearly 60% of the soluble cytosol proteins in neutrophils and plays a central role in neutrophil defense. Upon neutrophil activation or endothelial adhesion of monocytes, calprotectin is released and may be detected in serum, body fluids or stool as a potentially useful clinical inflammatory marker. The acute phase protein shows a high stability in feces (stable for one week at room temperature) and has been established as a fecal marker of inflammatory bowel diseases (IBD). It allows a reliable differentiation between organic intestinal diseases (e.g. chronic inflammatory diseases, infectious diseases, polyps, colon cancer) and functional intestinal diseases (e.g. irritable bowel syndrome).

Calprotectin is ideal for monitoring disease activity (e.g. of M. Crohn or after polyp resection) and early detection of relapse. It shows high sensitivity in the detection of colorectal carcinoma (CC) and polyps (CRC: sensitivity 100%, polyps: sensitivity 88%). Calprotectin further was qualified for discriminating between an organic diarrhoea and a functional diarrhoea.

## Principle

The test device is composed of a sample well and an oval result window. In the result window one, two or three colored lines could be seen after the test has been performed.

## Materials Provided

One **PreventID® CalDetect** test kit contains the following items to perform the test:

1. **PreventID® CalDetect** test device (with drying agent, not required for test)
2. Stool sample collection device with extraction buffer solution and sample collection stick
3. Paper faecal sample collection strip with instruction sheet for sample collection
4. Instruction manual

## Materials required but not provided

Timer or stop watch

## Reagent Storage

Store all reagents at 4 - 30°C. Beware: The interpretation time is based on reading the test results at room temperature (15-30°C). If the test device or the extraction buffer were stored at lower temperatures make sure they are at room temperature before starting the test. All reagents are provided ready to use.

## Precautions

1. For *in vitro* diagnostic use only.
2. Do not use beyond the expiration date.
3. Do not open the aluminum-laminated wrapper until you are ready to perform the test.
4. Do not use test device if the aluminium pouch is torn or if the membrane of the rapid test device is visibly damaged.
5. Used test devices, sample diluent, and sample collection device should be disposed of according to appropriate guidelines of biohazardous waste.
6. If you have questions please contact the manufacturer or distributor.

## Specimen collection

1. The faecal sample is directly collected in flat-pan toilets or in the case of funnelled toilets according to the printed instructions on the paper sample collection strips.
2. Unscrew the cap of the sample collection device and stick the attached collection stick into the faeces (approximately 2 cm).
3. Retract the sample collection stick with the adhering faecal sample and insert it into the collection device containing an extraction buffer solution. Screw cap on firmly and shake well.
4. Repeat steps 2 and 3.
5. If **PreventID® CalDetect** rapid test is not run within one day of sample collection, the sample collection device should be stored at 2 - 8°C, but for not more than 7 days.

## Test procedure

1. Remove test from its pouch and place on a flat dry surface. The oval sample opening at the one end of the test device should be at the right side (Fig. 1)
2. Label the device with patient name or identification number.
3. After the sample collection procedure has been completed, break off the tip of the sample collection device carefully (avoid dripping). Store specimen collection tube in a container to prevent the test solution from falling over. Squeeze **3 drops** of the extracted sample into the sample opening on the right site of the test device.
4. In a properly working test, a violet band will pass through the square result window in the middle of the test device. In the case you see no color band passing through the result window, add 1 more drop.
5. The result should be interpreted **3 minutes** after the last drop has been placed.

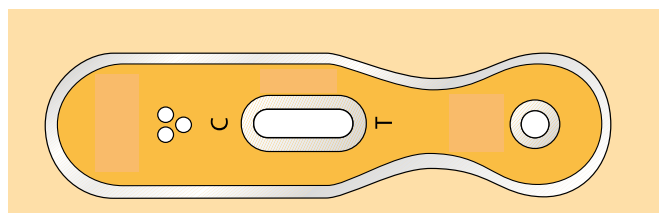


Fig. 1: **PreventID® CalDetect** Test device

## Interpretation of the Test Result (Figure 2)

### Negative

**Calprotectin not detectable:** A solitary control line (C) in the result window indicates that the test has run correctly.

**Calprotectin ≤ 15 µg/g:** The presence of **two color bands** (C and T1) within the result window indicates a calprotectin concentration of ≤ 15 µg/g. There is no bowel inflammation.

### Positive

**Calprotectin concentration 15 - 60 µg/g:** The presence of **3 color bands** (C, T1, T2) within the result window indicates a calprotectin concentration between 15 µg/g and 60 µg/g. An inflammatory process is going on in the mucosa.

**Calprotectin concentration > 60 µg/g:** The presence of **4 color bands** (C, T1, T2, T3) within the result window indicates a calprotectin concentration higher than 60 µg/g. A high-grade inflammatory process is going on in the mucosa

### Invalid

If, after conducting the test, neither of the colour bands are visible or only a test band (T) is visible, the test is **invalid**.

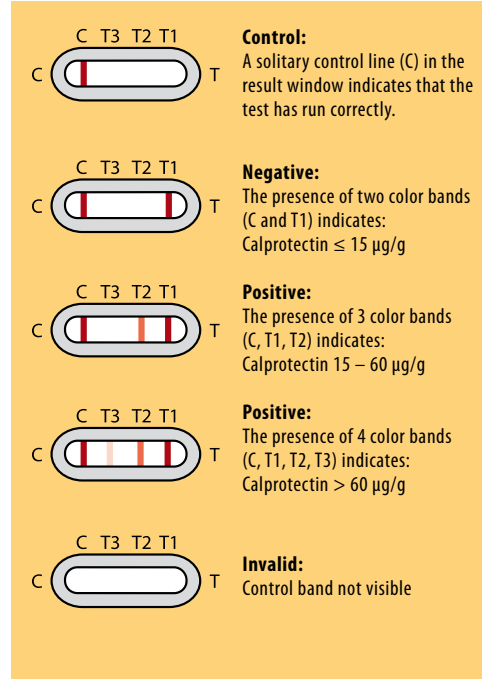


Fig. 2: Interpretation of Test Result

## Limitations of the Test

Although the **PreventID® CalDetect** is very accurate in detecting calprotectin a low incidence of false results can occur. Other clinically available tests are required if questionable results are obtained.

As with all diagnostic tests, a definitive clinical diagnosis should not be based on the results of a single test, but should only be made by the physician after all clinical and laboratory findings have been evaluated.

## Literature

Bergis D et al. (2005) Verdacht auf infektiöse Diarrhoe - Stuhlkultur ja oder nein? Evaluierung eines Stuhl-Calprotectinschnelltestes als positiver prädiktiver Marker für invasive Erreger. Z Gastroenterol 43: 948 (P512)

Gaya DR et al. (2005) Faecal calprotectin in the assessment of Crohn's disease activity. QJM 98: 435-441

Schröder O et al. (2007) Prospective evaluation of faecal neutrophil-derived proteins in identifying intestinal inflammation: combination of parameters does not improve diagnostic accuracy of calprotectin. Alimentary Pharmacology & Therapeutics. Postprint; doi: 10.1111/j.1365-2036.2007.03457.x

Shastri Y et al. (2006) Comparative study of new rapid bedside fecal calprotectin test with an established ELISA to assess intestinal inflammation in a prospective study. Gastroenterology 130 (4): AGA Abstracts: A-200

Striz I, Trebichavsky IL (2004) Calprotectin - a pleiotropic molecule in acute and chronic inflammation. Physiol Res. 53: 245-253 (Review)

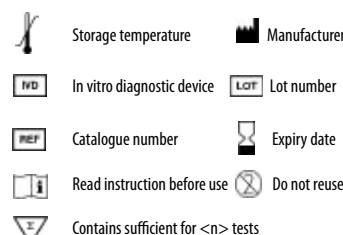
Tibble JA et al. (2000) A simple method for assessing intestinal inflammation in Crohn's disease. Gut 47: 506-513

Tibble JA et al. (2002) Use of surrogate markers of inflammation and Rome criteria to distinguish organic from nonorganic intestinal disease. Gastroenterology 123: 450-460

## Short Instruction for the handling of the PreventID® CalDetect

1. Collect the faecal samples by the aid of the sample collection device and the sample collection stick as described in the instruction.
2. Shake the solution in the sample collection device very thoroughly. Unpack the test unit.
3. Break off the tip of the sample collection device carefully.
4. Squeeze **three drops** of the extracted sample into the round sample opening.
4. Read the findings of the test **after 3 minutes**.

As of August 2007



## GASTROENTEROLOGY

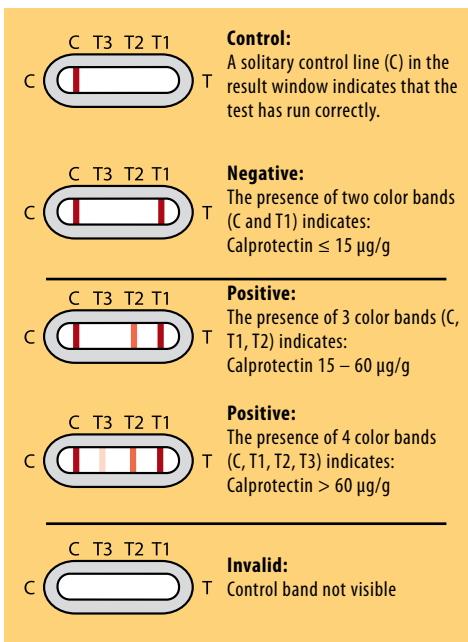
You may receive more information to this and other point-of-care tests on demand.

### Discrimination between organic and functional diarrhoea

Calprotectin is also qualified for discriminating between an organic diarrhoea and a functional diarrhoea as well as a positive predictive marker for an infectious diarrhoea. Increased calprotectin concentrations ( $> 15 \mu\text{g/g}$ ) indicate invasive pathogens as causative of diarrhoea.

#### Simple test procedure of the PreventID® CalDetect

- Collect a stool sample (in accordance to the instructions) in the sample collection tube before performing the test.
- Apply drops of the dissolved stool sample
- Wait 3 minutes to read the test result in the result window



### Interpretation of the test result

#### Negative

**Calprotectin not detectable:** A solitary control line (C) in the result window indicates that the test has run correctly.

**Calprotectin  $\leq 15 \mu\text{g/g}$ :** The presence of two color bands (C and T1) within the result window indicates a calprotectin concentration of  $\leq 15 \mu\text{g/g}$ . There is no bowel inflammation.

#### Positive

**Calprotectin concentration  $15 - 60 \mu\text{g/g}$ :** An inflammatory process is going on in the mucosa.

**Calprotectin concentration  $> 60 \mu\text{g/g}$ :** A high-grade inflammatory process is going on in the mucosa.

#### References

Gaya DR et al. (2005) Faecal calprotectin in the assessment of Crohn's disease activity. QJM 98: 435-441

Schröder O et al. (2007) Prospective evaluation of faecal neutrophil-derived proteins in identifying intestinal inflammation: combination of parameters does not improve

diagnostic accuracy of calprotectin. Alimentary Pharmacology & Therapeutics. Postprint; doi: 10.1111/j.1365-2036.2007.03457.x

Shastri Y et al. (2006) Comparative study of new rapid bedside fecal calprotectin test with an established ELISA to assess intestinal inflammation in a prospective study. Gastroenterology 130 (4): AGA Abstracts: A-200

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LID	PhiCal CO=50 µg/g	Buhlmann CO=50 µg/g	ImmunoD. CO=15µg/g	Preventis ND	Preventis T1: < 15 ug/g	Preventis T1+T2: 15 - 60 ug/g	Preventis T1+T2+T3: > 60 ug/g
6654409	15,2	18,2	6,2	x			
6655094	9,9	8,6	6,7	x			
6487729	6,1	5,9	7,0	x			
6657142	11,1	12,4	7,1	x			
6484983	18,3	5,3	9,9	x			
6883495	19,6	23,4	10,4	x			
6883494	13,8	22,7	11,3	x			
6893211	4,6	5,9	11,4	x			
6893457	17,9	28,1	12,3	x			
6654408	20,9	19,2	16,5			x	
21160549	20,6	44,5	21,4	x			
13147428	28,8	44,8	24,7			x	
6654135	20,4	36,3	25,1			x	
6893209	39,0	24,5	26,0			x	
6893458	12,4	18,3	26,2			x	
6883492	32,0	61,0	26,9			x	
6893201	48,8	89,0	30,6			x	
13141617	45,9	81,0	33,4			x	
6893179	42,4	74,6	38,8			x	
13142196	46,6	60,6	41,0			x	
6893189	150,0	207,0	102,0			x	
6883496	187,0	369,0	102,0				x
6655093	134,0	188,2	125,0				x
6893462	736,0	319,0	224,0				x
6893212	847,0	1365,0	233,0				x
6893213	1204,0	2075,0	289,0				x
6652700	1656,0	925,0	303,0				x
6653117	1765,0	1513,0	332,0				x
6656037	788,0	587,0	335,0				x
13127708	1614,0	926,0	391,0				x
90068941	1063,0	3125,0	952,0				x
6654182	2002,0	2080,0	1144,0				x
6654133	8930,0	9503,0	6115,0				x

PhiCal				Buhlmann			
PreventID	+	-		PreventID	+	-	
+	13	10	23	+	18	5	23
-	0	10	10	-	0	10	10
	13	20	33		18	15	33

Sensitivity: 100%  
Specificitet: 50%

Sensitivity: 100%  
Specificitet: 67%

ImmunoD.				PhiCal			
PreventID	+	-		Buhlmann	+	-	
+	23	0	23	+	13	5	18
-	1	9	10	-	0	15	15
	24	9	33		13	20	33

Sensitivity: 96%  
Specificitet: 100%

Sensitivity: 100%  
Specificitet: 75%

PhiCal				Buhlmann			
ImmunoD	+	-		ImmunoD	+	-	
+	13	11	24	+	18	6	24
-	0	9	9	-	0	9	9
	13	20	33		18	15	33

Sensitivity: 100%  
Specificitet: 45%

Sensitivity: 100%  
Specificitet: 60%

