510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K190784

B. Purpose for Submission:

New Device

C. Measurand:

Fecal calprotectin

D. Type of Test:

Quantitative, Particle-enhanced turbidimetric immunoassay (PETIA)

E. Applicant:

BÜHLMANN Laboratories AG

F. Proprietary and Established Names:

BÜHLMANN fCAL turbo

G. Regulatory Information:

1. Regulatory Section:

   21 CFR 866.5180, Fecal calprotectin immunological test system

2. Classification:

   Class II

3. Product Code:

   NXO, Calprotectin, Fecal

4. Panel:

   Immunology (82)

H. Intended Use:

1. Intended use:

   The BÜHLMANN fCAL turbo is an in vitro diagnostic assay intended for the quantitative measurement of fecal calprotectin, a neutrophilic protein that is a marker of intestinal mucosal inflammation, in human stool. The BÜHLMANN fCAL turbo 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.

2. Indication for use:

   Same as Intended Use

3. Special conditions for use statement:

   Prescription use only

4. Special instrument requirements:

   Roche cobas c501/c502 platforms

I. Device Description:

The BÜHLMANN fCAL turbo kit contains the following materials (96 tests):

- Reaction Buffer (R1) (1 vial, 35 mL)
- Immunoparticles (R2) (1 vial, 7 mL)

The following materials are required for the assay but not included in the BÜHLMANN fCAL turbo kit:

- BÜHLMANN fCAL turbo Calibrator Kit: Calibrator 1-6 (1 vial/calibrator, 1mL each, total 6 vials)
- BÜHLMANN fCAL turbo Control Kit: Low and High Control (3 vials/control, 1 mL each, total 6 vials)
- Stool Extraction buffer (125 mL/bottle)

J. Substantial Equivalence Information:

1. Predicate device name:

   BÜHLMANN fCAL ELISA

2. Predicate 510(k) number:

   K181012

3. Comparison with predicate:

Similarities		
Item	**BÜHLMANN fCAL turbo**	**BÜHLMANN fCAL ELISA (K181012)**
Intended Use	The BÜHLMANN fCAL turbo is an in vitro diagnostic assay intended for the quantitative measurement of fecal calprotectin, a neutrophilic protein that is a marker of intestinal mucosal inflammation, in human stool. The BÜHLMANN fCAL turbo 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.	The BÜHLMANN fCAL ELISA is an in vitro diagnostic assay intended for the quantitative measurement of fecal calprotectin in human stool. 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.
Analyte	Human fecal calprotectin (MRP8/14)	Same
Assay format	Quantitative	Same
Specimen type	Human stool	Same
Extraction Method	Manual Weighing (1:50 dilution in Extraction Buffer)	Same
Clinical Decision Thresholds	Normal: < 80 µg/g Gray-zone: 80–160 µg/g Elevated: > 160 µg/g	Same

Differences		
Item	**BÜHLMANN fCAL turbo**	**BÜHLMANN fCAL ELISA (K181012)**
Method	PETIA	ELISA
Automation	Automated	Manual
Solid Phase	Polystyrene nanoparticles (beads)	96-well polystyrene microtiter plate
Detection Method	Automated clinical chemistry analyzer read at 546 nm	Microtiter plate reader read at 450 nm
Analyte-specific antibody components	Polyclonal antibodies against human calprotectin coated on polystyrene beads	Capture antibodies: monoclonal antibodies against human calprotectin coated on microtiter plates Detection antibodies: monoclonal antibodies against human calprotectin conjugated to HRP
Measuring range	30–2,000 µg/g	30–1,800 µg/g
Expected Measuring Range (1:10 dilution)	30–10,000 µg/g	N/A
Calibrators	6 levels: Target values: 0, 50, 200, 500, 1000, 2000 µg/g	5 levels: 4, 12, 40, 120, and 240 ng/mL
Calibrator Source	Native human calprotectin from human granulocyte extract	Native human calprotectin from human serum

K. Standard/Guidance Documents Referenced:

- CLSI EP05-A3 Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition
- CLSI EP6-A Evaluation of The Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline
- CLSI EP07-A2 Interference Testing in Clinical Chemistry; Approved Guideline – Second

Edition

- CLSI EP10-A2 Preliminary Evaluation of Quantitative Clinical Laboratory Measurement Procedures Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition
- CLSI EP17-A2 Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition
- CLSI EP25-A Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline

L. Test Principle:

The BÜHLMANN fCAL turbo test is a particle-enhanced turbidimetric immunoassay (PETIA) which allows for automated quantification of calprotectin in fecal extracts on clinical chemistry analyzers. Fecal samples are extracted with extraction buffer using the manual weighing method and applied at a final dilution of 1:500. The extracts are incubated with reaction buffer and mixed with polystyrene nanoparticles coated with calprotectin-specific antibodies (immunoparticles). Calprotectin available in the sample mediates immunoparticle agglutination. Sample turbidity, measured by light absorbance, increases with calprotectin-immunoparticle complex formation and is proportional to calprotectin concentration. The detected light absorbance allows quantification of calprotectin concentration via interpolation on an established calibration curve.

M. Performance Characteristics:

1. Analytical performance: All studies presented below met the manufacturer's pre-determined acceptance criteria.

   a. Precision/Reproducibility:

   Precision: Eight extracted stool samples of various concentrations of calprotectin were tested for 20 days with two runs per day in two replicates per run, for a total of 80 BÜHLMANN fCAL turbo test results per sample. The mean BÜHLMANN fCAL turbo test result was computed and the within-run, between-run, between-day, and total standard deviations (SD) and associated coefficients of variation (%CV) were calculated.

Sample	Mean (µg/g)	Within-Run		Between-Run		Between-Day		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	42.9	3.6	8.3	1.2	2.7	1.1	2.5	3.9	9.1
2	98.4	2.5	2.6	1.8	1.8	2.2	2.2	3.7	3.8
3	166.5	4.3	2.6	0.8	0.5	1.9	1.2	4.8	2.9
4	267.6	3.9	1.4	2.5	0.9	1.8	0.7	5.0	1.9
5	642.0	20.1	3.1	14.9	2.3	0.0	0.0	25.1	3.9
6	1414.2	19.6	1.4	11.1	0.8	3.5	0.2	22.8	1.6
7	3251.4	40.8	1.3	21.4	0.7	19.7	0.6	50.1	1.5
8	5405.6	40.2	0.7	56.6	1.0	34.5	0.6	77.5	1.4

Reproducibility: To evaluate between-operator imprecision and between-site reproducibility, eight extracted stool samples at various concentrations of calprotectin were tested for five days with one run per day in five replicates per run at three sites, allowing for a total of 75 BÜHLMANN fCAL turbo test results per sample. The mean BÜHLMANN fCAL turbo test result was computed and the within-run, between-day, between-site, and total standard deviations (SD) and associated coefficients of variation (%CV) were calculated.

Sample	Mean (µg/g)	Within-run		Between-day		Between-site		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	47.2	3.6	7.6	2.4	5.0	0.0	0.0	4.3	9.1
2	91.1	3.5	3.8	3.5	3.8	2.8	3.1	5.7	6.2
3	185.4	5.1	2.7	2.7	1.4	5.5	3.0	7.9	4.3
4	276.9	6.4	2.3	4.5	1.6	9.7	3.5	12.5	4.5
5	674.5	12.9	1.9	1.2	0.2	22.8	3.4	26.3	3.9
6	1519.6	25.3	1.7	17.8	1.2	62.3	4.1	69.6	4.6
7	3343.8	54.6	1.6	35.6	1.1	100.0	3.0	119.4	3.6
8	5475.6	72.1	1.3	35.8	0.7	154.2	2.8	173.9	3.2

To evaluate between-lot imprecision, eight extracted stool samples of various concentrations of calprotectin were tested for five days in five replicates and three lots, for a total of 75 BÜHLMANN fCAL turbo test results per sample. The mean BÜHLMANN fCAL turbo test result was computed and the within-run, between-run, between-day, and total standard deviations (SD) and associated coefficients of variation (%CV) were calculated.

Sample	Mean (µg/g)	Within-run		Between-day		Between-lot		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	45.2	3.2	7.1	1.4	3.0	3.7	8.2	5.1	11.3
2	86.4	3.7	4.3	1.2	1.4	5.7	6.6	6.9	7.9
3	175.8	5.0	2.9	0.3	0.2	9.9	5.6	11.1	6.3
4	263.9	7.6	2.9	0.0	0.0	10.0	3.8	12.5	4.7
5	647.4	15.5	2.4	0.0	0.0	15.3	2.4	21.7	3.4
6	1460.7	33.7	2.3	11.6	0.8	41.0	2.8	54.3	3.7
7	3234.5	71.2	2.2	8.9	0.3	130.3	4.0	148.8	4.6
8	5303.1	97.4	1.8	11.2	0.2	163.9	3.1	191.0	3.6

To evaluate extraction reproducibility, stool samples in three different categories of stool consistency with one liquid (Sample 6), four semi-solid (Sample 1, 4, 7, and 10), and five solid samples (Sample 2,3,5,8, and 9) were extracted manually extracted by two operators for two days, tested in four extractions, and measured in five replicates per extraction, for a total of 80 BÜHLMANN fCAL turbo test results obtained per sample. For each sample, the means BÜHLMANN fCAL turbo test results were calculated and the within-extraction, between-extraction, and total standard deviations (SD) and associated coefficients of variation (%CV) were calculated.

Sample	Mean (µg/g)	Within-run		Between-extraction		Between-day		Between-operator		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	47.7	2.8	5.9	1.1	2.4	0.7	1.5	1.4	2.9	3.4	7.2
2	72.3	3.8	5.2	3.9	5.4	4.2	5.8	0.0	0.0	6.8	9.5
3	96.1	3.8	3.9	2.2	2.3	1.4	1.4	0.0	0.0	4.6	4.8
4	170.6	4.0	2.4	2.5	1.5	8.7	5.1	0.0	0.0	9.9	5.8
5	277.0	3.7	1.4	27.9	10.1	10.0	3.6	11.0	4.0	31.8	11.5
6	421.1	9.8	2.3	5.9	1.4	15.3	3.6	0.0	0.0	19.1	4.5
7	573.9	5.4	0.9	39.5	6.9	0.0	0.0	0.0	0.0	39.9	6.9
8	1387.4	39.1	2.8	75.1	5.4	159.9	11.5	0.0	0.0	180.9	13.0
9	3264.9	87.2	2.7	236.2	7.2	256.9	7.9	0.0	0.0	359.7	11.0
10	3330.4	89.8	2.7	92.4	2.8	75.7	2.3	0.0	0.0	149.4	4.5

b. Linearity/assay reportable range:

Linearity: A linearity study was conducted in accordance with CLSI guideline EP6-A. Two sample pools were prepared to obtain 15 concentration levels per sample pool to cover the full range of the assay from 30 µg/g to 2,000 µg/g (30 µg/g to 10,000 µg/g for samples with an additional dilution) calprotectin. Four replicates were obtained at each concentration level to cover the assay measuring range.

Sample	Range (µg/g)	Slope (95%CI)	Intercept (95% CI)	R^2
1	37.6–12,216.0	1.06 (1.04, 1.08)	5.7 (1.6, 16.9)	0.998
2	33.5–13,339.5	1.03 (1.01, 1.04)	3.8 (-0.4, 13.3)	0.998

Accuracy/Recovery: To evaluate the accuracy of the BÜHLMANN fCAL turbo, seven stool specimen extracts were spiked with calprotectin calibrators at a defined concentration of 500 µg/g for Sample 1–4 and 2,000 µg/g for Samples 5–7 in 10% specimen extract volume, corresponding 50 µg/g for Sample 1–4 and 200 µg/g for Samples 5–7. Four replicates were obtained per each sample.

Specimen Extract	Mean Baseline Result (µg/g)	Spiked Value (µg/g)	Expected Post-Spike Result (µg/g)	Observed Post-Spike Result (µg/g)	Recovery (%)
1	44.1	56.9	101.0	94.6	93.6
2	65.5	56.9	122.4	114.5	93.6
3	116.4	56.9	173.3	170.2	98.2
4	138.5	56.9	195.4	186.9	95.7
5	230.9	227.8	458.7	453.1	98.8
6	510.8	227.8	738.6	753.2	102.0
7	1076.3	227.8	1304.1	1309.3	100.4

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Traceability:
No international reference material or reference measurement procedures are available for calprotectin. Therefore, metrological traceability to international (SI) units cannot be established. The BÜHLMANN fCAL turbo is traceable to an internal standard generated by mixing a recombinant calprotectin antigen (MRP8/14 dimer) with the BÜHLMANN B-CAL-EX extraction buffer. Final value assignment was performed with the BÜHLMANN fCAL turbo using multiple reagent lots.

Stability:
Real-time reagent stability: Three reagent lots and four stool extracts (one below 80 µg/g, one between 80 µg/g and 160 µg/g, and two above 160 µg/g) were used to establish reagent stability. Reagents were stored at 2–8°C throughout the study. Stool extracts were stored in accordance with the instructions for use. The results of the study support the claim that BÜHLMANN fCAL turbo reagents are stable for six months at 2–8°C.

Transport stability: Four stool samples and two levels of control material were used. Reagents were stored at 28°C and 37°C to mimic temperature conditions that may be experienced during shipping. Reagent/sample/control combinations were tested in duplicates at baseline, and at seven days, 14 days, 21 days, and 28 days post-baseline. The results of the study support the claim that BÜHLMANN fCAL turbo reagents are stable for 28 days at 37°C.

On board stability: One reagent lot, four stool samples, and two levels of control material were used to evaluate on board stability. The reagents were opened and reconstituted prior to testing at baseline then stored at 5–12°C and used at 2, 4, 6, 8, 10, 12, and 13 weeks after the baseline time point. The results of the study support the claim that the BÜHLMANN fCAL turbo reagents are stable for 12 weeks in open kit/in-use.

Analyte stability: Analyte stability was evaluated under the following storage conditions of:

- raw stool specimens at 2–8°C
- stool extracts at -20°C and 2–8°C

The demonstrated stability duration is four days at 2–8°C for raw stool specimen, two months at -20°C for stool extract, and 11 days at 2–8°C for stool extract.

d. Detection limit:

Limit of Blank (LoB)
Four blank samples (extraction buffer) were tested over a three-day period using five replicates in two reagent lots. The study design generated a total of 60 test determinations with each reagent lot and the LoB was estimated as the 95th percentile of the distribution of test results using a non-parametric method. The higher estimate obtained with one lot was used as the claimed LoB. The LoB value was determined to be 16.7 μg/g.

Limit of Detection (LoD)
Four specimen extracts with low levels of calprotectin were tested over three days with each sample tested in five replicates. The study design generated a total of 60 test determinations with each reagent lot. The LoD was calculated using parametric analysis. The study was conducted independently with two reagent lots and the higher estimate obtained with one lot was used as the claimed LoD. The LoD value was determined to be 23.7 μg/g.

Limit of Quantitation (LoQ)
The LoQ was established with six specimen extracts at low calprotectin levels. The samples were measured over three days in five replicates each day to generate a total of 90 replicates. The study was conducted independently with two reagent lots. The mean test result and associated coefficient of variation (%CV) were computed for the lowest calprotectin concentration with imprecision below 20 %CV. The LoQ value was determined to be 30.0 μg/g.

e. Analytical specificity:
A total of 19 potential interferents were investigated in this study, including six microorganisms and 13 chemical interferents (e.g., oral pharmaceuticals and nutritional supplements) with four samples with calprotectin concentrations at: near 30.0 μg/g, 100.0 μg/g, 300.0 μg/g, and 550.0 μg/g are listed in the tables below:

Microorganism interferences:

Microorganism	Concentration (cfu/mL)
Escherichia coli	3.3×10^7
Salmonella enterica subsp. enterica	9.0×10^7
Klebsiella pneumoniae subsp. pneumonia	5.3×10^7
Citrobacter freundii	12.9×10^7
Shigella flexneri	5.0×10^7
Yersinia enterocolitica subsp. enterocolitica	9.8×10^7

Drugs and endogenous factor interferences:

Trade name	Active component	Concentration (mg/50 mg stool)
gyno-Tardyferon	Iron (II) sulfate	0.11
Prednisone	Prednisone	0.31
Imurek	Azathioprine	0.19
Salofalk	Mesalamine; 5-ASA	5.21
Agopton	Lansoprazole	0.18
Asacol	Mesalamine; 5-ASA	2.50
Vancocin	Vancomycin	2.00
Sulfamethoxazol	Sulfamethoxazole	1.60
Trimethoprim	Trimethoprim lactate	0.35
Ciproxine	Ciprofloxacin	1.25
Vitamin E	DL-α Tocopherol Acetate	0.30
Bion 3	Multivitamin	1.06
Hemoglobin	Hemoglobin	1.25

The tested potential interferents exhibited a change of <10% in the mean BÜHLMANN fCAL turbo test results when added to stool specimen extracts at various levels of fecal calprotectin.

f. Assay cut-off:

The assay cut-offs for the BÜHLMANN fCAL turbo are:

Calprotectin Concentration	Interpretation	Follow-Up
< 80 μg/g	Normal	None
80 μg/g ≤ x ≤ 160 μg/g	Gray-zone/Borderline	Retest within 4–6 weeks
> 160 μg/g	Elevated	Repeat as needed

g. Carry over:

Three sample pools (low, medium, and high) were tested over 5 days, in one run per day, with three results generated per sample pool per run. One reagent lot was used in the study. No sample carry-over with the BÜHLMANN fCAL turbo test on Roche cobas 6000 c501 instrument was detected.

2. Comparison studies:

a. Method comparison with predicate device:

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A total of 248 samples were obtained for the method comparison study; samples with the test results within the measuring range for both BÜHLMANN fCAL ELISA and BÜHLMANN fCAL turbo (n = 220) were included in the regression analysis. The study subject population consisted of: 76 samples from patients with IBD (61 adults and 15 pediatric); 56 samples from patients with IBS (43 adults and 13 pediatric); 32 samples from patients with other GI conditions (30 adults and 2 pediatric); and 56 samples from normal healthy adults. The linear regression analysis obtained from Passing-Bablok regression analysis comparing BÜHLMANN fCAL turbo test results to corresponding BÜHLMANN fCAL ELISA test results is shown below:

Lot	**N**	**Range (µg/g)**	**Slope (95% CI)**	**Intercept (95% CI)**	**R**	**% Bias at 80 µg/g (95% CI)**	**% Bias at 160 µg/g (95% CI)**
All	220	30.6–1,763.9	1.025 (0.990–1.058)	-4.5 (-8.7–0.3)	0.972	-3.1 (-7.2–0.5)	-0.3 (-2.4–2.7)
1	74	30.6–1,120.4	1.026 (0.951–1.086)	-7.3 (-16.4–0.5)	0.975	-6.5 (-13.4 to -0.2)	-1.9 (-7.1–3.2)
2	73	32.1–1,421.6	0.996 (0.951–1.052)	-3.2 (-12.4–1.6)	0.974	-4.5 (-14.7 to -0.6)	-2.5 (-8.0–0.5)
3	73	35.1–1,763.9	1.045 (0.987–1.120)	0.1 (-8.0–6.6)	0.975	4.6 (-1.4–11.4)	4.5 (0.4–10.2)

All 248 samples were used in a qualitative assessment of the assay. The study subject population consisted of 77 samples from patients with IBD, 65 samples from patients with IBS, 37 samples from patients with other GI conditions, and 69 samples from normal healthy adults and were additionally tested for agreement analysis using

BÜHLMANN fCAL turbo and the predicate assay (BÜHLMANN fCAL ELISA) in accordance with each assay's instructions for use. The comparison analysis was performed using cut-offs of both assays and the number of study subjects at each level.

		Subject number in BÜHLMANN fCAL ELISA range (µg/g)			
		< 80	**80–160**	**> 160**	**Total**
Subject number in BÜHLMANN fCAL turbo range (µg/g)	**< 80**	84	10	0	94
	80–160	8	41	6	55
	> 160	0	7	92	99
Total		92	58	98	248

Estimates of percent agreement, positive percent agreement (PPA) and negative percent agreement (NPA), between BÜHLMANN fCAL ELISA and BÜHLMANN fCAL turbo assay results area shown below:

Metric	**Estimate**	**95% C.I.**
PPA at 80µg/g cutoff	146/156 = 93.6%	[88.5%, 96.9%]
NPA at 80µg/g cutoff	84/92 = 91.3%	[83.6%, 96.2%]
PPA at 160µg/g cutoff	92/98 = 93.9%	[87.1%, 97.7%]
NPA at 160µg/g cutoff	143/150 = 95.3%	[90.6%, 98.1%]

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical Sensitivity/clinical specificity:

The study subject population consisted of 337 subjects including 274 adults (above age 21) and 63 pediatric (age between 4 and 21) patients. Per standard clinical practice, all patients presenting with signs and symptoms suggestive of IBS or IBD, including patients previously diagnosed with IBD and referred for endoscopic investigation due to a suspected flare or routine exam, were enrolled and referred for endoscopy. The final clinical diagnosis of IBD, IBS, or other GI disorder was determined by the clinical investigator based on the results of the endoscopy as well

as other clinical findings, e.g. histology and Rome III criteria. The final diagnoses of the subjects were as follows: 135 IBD (102 adult and 33 pediatric), 130 IBS (102 adult and 28 pediatric), and 72 other gastrointestinal disorders other than IBD or IBS (70 adults and 2 pediatric). Thirteen clinical sites in the U.S. enrolled and determined the final clinical diagnoses.

Final Diagnosis	**Subject number and percent in BÜHLMANN fCAL turbo range (µg/g)**			
	<80	**80-160**	**>160**	**Total**
IBD	12 (8.9%)	15 (11.1%)	108 (80.0%)	135 (100%)
IBS	99 (76.2%)	15 (11.5%)	16 (12.3%)	130 (100%)
GI Other	51 (70.8%)	7 (9.7%)	14 (19.4%)	72 (100%)

IBD vs. non-IBD comparison:

Estimates of sensitivity and specificity along with 95% confidence intervals were calculated for the BÜHLMANN fCAL turbo as an aid in diagnosis of IBD by comparing the test results between IBD and non-IBD (IBS and other gastrointestinal disorders) patients at ≥ 4 years of age, using test cutoffs at 80 and160 µg/g.

Positive cases considered at ≥80 µg/g		**Clinical Diagnosis**		**Total**
		IBD	**Non-IBD**	
BÜHLMANN fCAL turbo	**Positive**	123	52	175
	Negative	12	150	162
	Total	135	202	337
Sensitivity = 91.1%; 95% C.I. (85.0%, 95.3%)				
Specificity = 74.3%; 95% C.I. (67.7%, 80.1%)				

Positive cases considered at ≥160 µg/g		**Clinical Diagnosis**		**Total**
		IBD	**Non-IBD**	
BÜHLMANN fCAL turbo	**Positive**	108	30	138
	Negative	27	172	199
	Total	135	202	337
Sensitivity = 80.0%; 95% C.I. (72.3%, 86.4%)				
Specificity = 85.1%; 95% C.I. (79.5%, 89.8%)				

IBD vs. IBS diagnosis:

Estimates of sensitivity and specificity along with 95% confidence intervals were calculated for the BÜHLMANN fCAL turbo as an aid in the discrimination between

IBD and IBS in all subjects (≥4years of age), using test cutoffs at 80 and 160 µg/g.

Positive cases considered at ≥80 µg/g		Clinical Diagnosis		Total
		IBD	IBS	
BÜHLMANN fCAL turbo	**Positive**	123	31	154
	Negative	12	99	111
	Total	135	130	265
Sensitivity = 91.1%; 95% C.I. (85.0%, 95.3%)				
Specificity = 76.2%; 95% C.I. (67.9%, 83.2%)				

Positive cases considered at ≥160 µg/g		Clinical Diagnosis		Total
		IBD	IBS	
BÜHLMANN fCAL turbo	**Positive**	108	16	124
	Negative	27	114	141
	Total	135	130	265
Sensitivity = 80.0%; 95% C.I. (72.3%, 86.4%)				
Specificity = 87.7%; 95% C.I. (80.8%, 92.8%)				

b. Other clinical supportive data (when a. is not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Stool samples were obtained from 141 healthy normal adults (≥ 21 years of age) with no symptoms or signs of gastrointestinal disease. The test results were categorized by the assay cut-offs below:

	Calprotectin level by BÜHLMANN fCAL turbo			
	< 80 µg/g	**80 - 160 µg/g**	**> 160 µg/g**	**Total**
Subject number (%)	106 (75.2%)	18 (12.8%)	17 (12.0 %)	141 (100 %)

N. Proposed Labelling:

The labelling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.