

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

k053383

B. Purpose for Submission:

This is a new device.

C. Measurands:

Gliadin and Tissue Transglutaminase

D. Type of Test:

Multiplex bead-based flow cytometric immunoassay

E. Applicant:

Biomedical Diagnostics (bmd) S.A.

F. Proprietary and Established Names:

FIDIS™ CELIAC

G. Regulatory Information:

1. Regulation section:

Gliadin - 21CFR§ 866.5750, Radioallergosorbent (RAST) Immunological Test System

Tissue Transglutaminase - 21CFR§ 866.5660, Antinuclear Antibody Immunological Test System

2. Classification:

Class II

3. Product code:

MST, Antibodies, Gliadin

MVM, Autoantibodies, Endomysial (Tissue Transglutaminase)

4. Panel:

Immunology (82)

H. Intended Use:

1. Intended use(s):

The FIDIS™ CELIAC kit is a semi-quantitative homogeneous fluorescent-based microparticles immunoassay using flow cytometry readings.

CELIAC IgA is designed for the detection of human IgA isotype antibodies directed against Gliadin and Tissue Transglutaminase Enzyme.

CELIAC IgG is designed for the detection of human IgG isotype antibodies directed against Gliadin and Tissue Transglutaminase Enzyme.

1. Indication(s) for use:

The presence of these antibodies can be used in conjunction with clinical findings to aid in the diagnosis of Celiac disease.

The FIDIS™ CELIAC kit is to be used on serum only and used on the FIDIS™ Analyzer, MLX Booster software and washer.

3. Special conditions for use statement(s):

This device is for prescription use only.

4. Special instrument requirements:

FIDIS™ Instrument (Luminex 100™plus FIDIS™ MLX-Booster Software)
Caris™ system (diluting/dispensing device), optional

I. Device Description:

The device consists of the following: color-coded sets of microspheres (ready-to-use). Each microsphere set is sensitized by the 2 antigens, gliadin and tissue transglutaminase (tTG); calibrator (ready to use); positive control (to be diluted); negative control (to be diluted); goat anti-human IgG or IgA conjugate coupled phycoerythrin (to be diluted) and 10x concentrated PBS-Tween (to be diluted with distilled water)

J. Substantial Equivalence Information:

1. Predicate device name(s):
QuantaLite™ IgA Gliadin, QuantaLite™ IgA tTG, Varelisa® IgG Gliadin and Celikey®TgG tTG
2. Predicate 510(k) number(s):
k964986, k982366, k041357 and k041173
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
	FIDIS™ CELIAC kit	QuantaLite™ IgA Gliadin QuantaLite™ IgA tTG Varelisa® IgG Gliadin Celikey®TgG tTG
Intended Use	Determination of IgG or IgA antibodies against gliadin and tTg	Individual determination
Sample type	Serum	Same
Type of test	Semi-quantitative	Same

Differences		
Item	Device	Predicate
Assay type	Flow Cytometer based	ELISA
Assay Format	Multiplexed	Individual assays
Sample Dilution	1:200	1:101
Substrate solution	None	TMB
Instrument	Luminometer (Luminex v. 100)	Spectrophotometer
Detection method	Fluorescence	Colorimetric
Conjugate	Phycoerythrin	HR peroxidase
Solid Phase Capture	Color-coded microspheres	Microwells
Antigens	Gliadin: native antigen tTG: recombinant human antigen	QuantaLite Gliadin IgA:purified gliadin antigen QuantaLite tTG IgA:native human tTG Varelisa Gliadin IgG: no information about origin

Differences		
Item	Device	Predicate
		Celikey IgG: recombinant human tTG

K. Standard/Guidance Document Referenced (if applicable):

None referenced.

L. Test Principle:

FIDIS™ CELIAC kit is a multiplexed semi-quantitative, fluorescent immunoassay performed on the FIDIS™ Instrument (Luminex 100™) with the MLX Booster software. Each antigen required for the assay is covalently coupled to an individual set of microspheres through its surface functional groups. The different sets of antigen-coupled microspheres are mixed together to constitute the final microspheres reagent and put into wells of a microtiter plate. CELIAC IgA allows the detection of anti-gliadin and anti-t TG IgA isotype antibodies. CELIAC IgG allows the detection of anti-gliadin and anti-t TG IgG isotype antibodies. Prediluted controls and diluted patient sera are added to separate wells allowing autoantibodies to bind to the immobilized antigens on the beads. After incubation, a wash step through a filtration process will remove the unbound antibodies. Then a phycoerythrin labeled anti-human IgG or IgA is added to each well and binds to any patient antibodies/antigen complexes on the microspheres. The samples are subsequently measured in the FIDIS Instrument. The flow cytometer discriminates the different bead sets as well as measures the fluorescent intensity of the conjugate on each bead. For each sample, the antibody titer for each antigenic specificity is interpolated against a calibration system.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

To evaluate intra-assay and inter assay reproducibility, eight samples were analyzed on the **FIDIS™ CELIAC**. For within-run, the eight samples were assayed 10 times in one run and for between-run; the eight samples were assayed 4 times per run for 6 runs. Results were as follows:

Antigen	Within-run		Between-run	
	Mean value	%CV	Mean Value	%CV
Gliadin IgA	12	8.0	16	15
	41	6	40	5
	43	6	37	7
	45	5	47	7
	152	4	153	4
	572	3	593	5
tTG IgA	16.9	8	16.1	12
	36	5	37	9
	49	5	49	7
	51	6	46	8
	174	3	180	6

	Within-run		Between-run	
	362	4	377	7
Gliadin IgG	1	14	1	15
	28	10	26	15
	46	3	47	5
	94	3	89	8
	171	3	151	11
	275	10	252	9
tTG IgG	8.9	11	7.5	15
	35	12	312	14
	43	7	36	14
	45	5	38	15
	210	6	188	11
	371	11	337	11

Precision of the assay using the optional automated CARIS system was assessed. For within-run, eight samples were assayed 10 times in one run and for between-run; eight samples were assayed 4 times per run for 6 runs. Results were as follows:

	Within-run		Between-run	
Antigen	Mean value	%CV	Mean Value	%CV
Gliadin IgA	27	15	25	14
	37	9	42	11
	40	15	38	8
	57	11	55	8
	67	8	61	7
	86	10	91	6
	127	7	127	6
	209	7	201	8
tTG IgA	26	8	31	10
	30	6	40	12
	39	9	30	8
	73	7	87	9
	87	5	100	8
	111	7	129	12
	204	4	231	8
	280	4	307	7
Gliadin IgG	29	10	29	8
	37	9	36	11
	41	7	40	8
	54	9	51	8
	62	9	60	7
	74	9	69	9
	82	9	79	7
	99	6	100	8
tTG IgG	25	3	25	6
	28	7	28	6
	31	6	34	8
	50	4	50	7
	57	9	59	8
	81	7	84	6
	97	7	101	6
	98	7	103	6

- b. *Linearity/assay reportable range:*
Linearity is not claimed for this assay.
- c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
An international reference material for these antibodies is not available. Calibrator titers are expressed in arbitrary units per mL (AU/mL for IgA and GU/mL for IgG).
- d. *Detection limit:*
Not applicable
- e. *Analytical specificity:*

Interfering substances

To evaluate the system for potential cross reactivity to other antibodies and interference from blood components, 24 samples for IgA and 25 samples for IgG isotypes were tested. High level of complement proteins were used but the specific kind of complement was not provided. A statement to avoid the use of abnormal concentration of these samples was added to the Limitations of the Procedure. The following results were obtained.

	Number of positive samples			
	Gliadin IgA	t TG IgA	Gliadin IgG	t TG IgG
Cryoglobulinemia N=2	-	-	-	-
Complement N=5	2	-	-	-
IgG monoclonal immunoglobulins N=1	-	-	-	-
IgM monoclonal immunoglobulins N=4	1	-	-	-
Rheumatoid Factor N=7	1	1	1	1
Plasma (sodium citrate) N=3	1	-	-	-
Hemolyzed sera N=3	-	-	-	2

- f. *Assay cut-off:*
Eighty (80) samples for the IgA isotype evaluation including 56 normal blood donor samples and 24 samples with potential biological interferences (see analytical specificity) and 99 samples for the IgG isotype evaluation including 74 normal blood donor and 24 samples with potential biological interferences (see analytical specificity) were run to establish the cut-offs for the assays. The following results were obtained and between these thresholds, results are considered borderline:

Percentile of the Distribution values	15 AU/mL or GU/mL	20 AU/mL or GU/mL
Gliadin IgA	70% (56/80)	84% (67/80)
tTG IgA	99% (89/90)	99% (89/90)
Gliadin IgG	95% (94/99)	98% (97/99)
tTG IgG	88% (87/99)	93% (92/99)

2. Comparison studies:

a. *Method comparison with predicate device:*

The tables below show the comparison of serum samples (N=249 for IgA and 251 for IgG) that were tested with the FIDIS™ CELIAC and the predicate devices. No information about age, gender, and clinical status was provided.

- 169 IgA and 251 IgG samples related to Celiac diseases
- 56 IgA and 74 IgG negative samples
- 24 IgA and 25 IgG samples with potential biological interferences

All borderline results with the two devices were considered negative.

Gliadin IgA		ELISA	
		Pos	Neg
FIDIS	Pos	73	21
Celiac	Neg	7	148

Positive % agreement: 91.25% (95% CI: 85.1% - 97.4 %%)

Negative % agreement: 87.57% (95% CI: 82.6% - 92.5%)

Overall % agreement: 88.75% (95% CI: 84.8% - 92.7%)

tTG IgA		ELISA	
		Pos	Neg
FIDIS	Pos	61	1
Celiac	Neg	4	183

Positive % agreement: 93.85% (95% CI: 88.0% - 99.7%)

Negative % agreement: 99.46% (95% CI: 98.4% - 100.0%)

Overall % agreement: 97.99% (95% CI: 96.2% - 99.7%)

Gliadin IgG		Elisa	
		Pos	Neg
FIDIS	Pos	118	19
Celiac	Neg	3	111

Positive % agreement: 97.52% (95% CI: 94.8% - 100.0%)

Negative % agreement: 85.38% (95% CI: 79.3% - 91.5%)

Overall % agreement: 91.24% (95% CI: 87.7% - 94.7%)

tTG IgG		Elisa	
		Pos	Neg
FIDIS	Pos	34	9
Celiac	Neg	3	205

Positive % agreement: 91.89% (95% CI: 83.1% - 100.0%)

Negative % agreement: 95.79% (95% CI: 93.1% - 98.5%)

Overall % agreement: 95.22% (95% CI: 92.6% - 97.6%)

A study was performed to compare the manual FIDIS™ CELIAC and the optional automated diluting/dispensing device CARIS™. The

comparison was performed on 30 samples for Celiac G and 31 samples on Celiac A. The following results were obtained:

Gliadin IgA		Manual FIDIS	
		Pos	Neg
CARIS FIDIS	Pos	10	2
	Neg	0	19

Positive % agreement: 100%

Negative % agreement: 90.5%

Overall % agreement: 93.5%

tTG IgA		Manual FIDIS	
		Pos	Neg
CARIS FIDIS	Pos	5	0
	Neg	0	26

Positive % agreement: 100%

Negative % agreement: 100%

Overall % agreement: 100%

Gliadin IgG		Manual FIDIS	
		Pos	Neg
CARIS FIDIS	Pos	26	1
	Neg	0	3

Positive % agreement: 100%

Negative % agreement: 75%

Overall % agreement: 96.7%

tTG IgG		Manual FIDIS	
		Pos	Neg
CARIS FIDIS	Pos	1	0
	Neg	0	29

Positive % agreement: 100%

Negative % agreement: 100%

Overall % agreement: 100%

The three discrepant results (two for IgA and one IgG) with the CARIS FIDIS were false positives.

b. Matrix comparison:

Serum is the only recommended matrix.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Expected values in the normal population should be negative.

N. Proposed Labeling:

The labeling 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.