510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k060380

B. Purpose for Submission:
This is a new device.

C. Measurands:
Anti-DNA Antibodies

D. Type of Test:
Multiplex bead-based flow cytometric immunoassay

E. Applicant:
Biomedical Diagnostics (bmd) S.A.

F. Proprietary and Established Names:
FIDIS™ dsDNA

G. Regulatory Information:
1. Regulation section:
   21CFR§ 866.5100, Antinuclear Antibody Immunological Test System
2. Classification:
   Class II
3. Product code:
   LSW, Anti-DNA Antibody, Antigen and Control
4. Panel:
   Immunology (82)

H. Intended Use:
1. Intended use(s):
   The FIDIS ™ dsDNA kit is a semi-quantitative homogeneous fluorescent-based microparticles immunoassay using flow cytometry readings. It is designed for the detection of antibodies directed against double stranded DNA.
1. Indication(s) for use:
   The presence of these antibodies can be used in conjunction with clinical findings to aid in the diagnosis of SLE.
   The FIDIS ™ dsDNA 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 coupled with dsDNA (ready-to-use); calibrator (ready to use); positive control (to be diluted); negative control (to be diluted); goat anti-human IgG coupled to phycoerythrin (to be diluted) and 10x concentrated PBS-Tween (to be diluted

with distilled water)

J. Substantial Equivalence Information:
   1. <u>Predicate device name(s):</u>
      Varelisa® dsDNA Antibodies
   2. <u>Predicate 510(k) number(s):</u>
      k950031
   3. <u>Comparison with predicate:</u>

Similarities		
Item	Device	Predicate
	FIDIS™dsDNA kit	Varelisa® dsDNA
Intended Use	Determination of IgG antibodies against dsDNA	Same
Sample type	Serum	Same
Type of test	Semi-quantitative	Same
Antigen	Recombinant dsDNA	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

K. Standard/Guidance Document Referenced (if applicable):
   None referenced.

L. Test Principle:
   FIDIS™ dsDNA is based on the use of distinct uniform size color-coded microspheres and a benchtop flow cytometer interfaced to digital signal processing hardware and software. A red diode laser beam in the flow cytometer classifies each set of microspheres on the basis of its unique fluorescence intensity (red to orange) thus identifying which analyte is being tested. At the same time, a green laser beam illuminates the external second molecule fluorescence to quantify the reaction related to the specific analyte.
   The test is performed in a 96 well blank microplate with a filtering membrane at the bottom of the wells. In the first step, the sample is distributed in each well containing the microspheres covalently coupled to dsDNA. If this sample contains the suspected antibodies, these antibodies bind to the antigen. After incubation, a wash step using a filtration process removes the unbound antibodies.

A phycoerythrin labeled anti-human IgG will bind to the captured antibodies. The reaction is then directly measured by the flow cytometer, which categorizes each set of microspheres according to its fluorescence color while simultaneously measuring the average fluorescence emitted by the conjugate. A calibration system permits the determination of the titer of each sample by interpolation for each antigenic specificity.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

    a. *Precision/Reproducibility:*

    To evaluate intra-assay and inter assay reproducibility, nine samples were analyzed on the FIDIS™ dsDNA. For within-run, the nine samples were assayed 10 times in one run and for between-run; the nine 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
dsDNA	23	3	24	6
	45	3	51	9
	46	3.8	53	8.3
	70	4.3	69	4.3
	84	12.2	90	11.3
	138	3.9	140	4.2
	162	4.8	199	7.4
	519	2.8	524	5.6
	579	7.6	709	11.8

    Precision of the assay using the optional automated CARIS system was assessed. For within-run, five samples were assayed 10 times in one run and for between-run; five 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
dsDNA	41	6.8	41	6.2
	70	4.5	67.7	7.2
	80	7.0	70.8	11.2
	94	8.9	98.3	10.4
	894	5.3	871.5	5.2

    b. *Linearity/assay reportable range:*
    Linearity is not claimed for this assay.

    c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
    The dsDNA values in the calibrator are established using the WHO International Standard for Anti-double stranded DNA (dsDNA), human code: WO/80. The WHO WO/80 standard is lyophilized powder and is reconstituted to a concentration of 200 IU/mL. Information leaflet from WHO (First International Standard for Antibodies for Anti Double-stranded DNA (dsDNA)) was provided.

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, 35 samples 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.

Samples	No of samples positive for dsDNA
Cryoglobulinemia N=5	0
Complement N=10	2
Hypergammaglobulinemia N=1	0
IgG monoclonal immunoglobulins N=3	0
IgM monoclonal immunoglobulins N=7	0
Rheumatoid Factor N=2	0
Plasma (sodium citrate)N =5	0
Hemolyzed sera N=2	0

f. *Assay cut-off:*
    Eighty five (85) samples including 50 normal blood donor samples and
    35 samples with potential biological interferences (see analytical
    specificity) were run to establish the cut-offs for the assays. The
    following results were obtained:

Percentile of the Distribution values	30 IU/mL	40 IU/mL
dsDNA	94.1% (80/85)	95.3% (81/85)

Between these thresholds, results are considered equivocal or borderline.
2. Comparison studies:
    a. *Method comparison with predicate device:*
        The table below shows the comparison of serum samples (N=400) that
        were tested with the FIDIS™ dsDNA and the predicate device**.** No
        information about age, gender, and clinical status was provided.
        -   109 positive samples for one or more parameters related to
            systemic autoimmune diseases
        -   291 negative samples
        -   All borderline results with the two devices were considered
            negative.

		Varelisa dsDNA	
		Pos	Neg
FIDIS dsDNA	Pos	105	13
	Neg	4	278

Positive % agreement: 96.33% (95% CI: 92.8 - 99.9 %)
Negative % agreement: 95.53% (95% CI: 93.2 – 97.9%)
Overall % agreement: 95.75% (95% CI: 93.8 – 97.7%)

A study was performed to compare the manual FIDIS™ dsDNA and the optional automated diluting/dispensing device CARIS™. The comparison was performed on 151 samples. The following results were obtained:

dsDNA		Manual FIDIS	
		Pos	Neg
CARIS FIDIS	Pos	58	3
	Neg	0	90

Positive % agreement: 100%
Negative % agreement: 96.8%
Overall % agreement: 98 %
The three discrepant samples with the CARIS FIDIS were false positives for dsDNA.

    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.