510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k102607

B. Purpose for Submission:
Modified device: Analyte name change from SS-A 52kDa to TRIM21 and the number of microspheres read per assay is reduced from 200 to 100 with an increase in read time.

C. Measurand:
Anti-dsDNA, anti-SSA (60kDA and TRIM 21 (SS-A 52kDA)), anti-SS-B, anti-Sm, anti-Sm/RNP, anti-Scl-70, anti-Jo-1, anti-ribosomes and anti-centromere)

D. Type of Test:
Semi-quantitative

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

F. Proprietary and Established Names:
FIDIS™ CONNECTIVE 10

G. Regulatory Information:

1. Regulation section:
   21 CFR § 866.5100, Antinuclear Antibody, immunological test systems
2. Classification:
   Class II
3. Product codes:
   LLL, Extractable Antinuclear Antibody, Antigen, and Control
   LKJ, Antinuclear Antibody, Antigen, and Control
   LKO, Anti-RNP Antibody, Antigen, and Control
   LKP, Anti-Sm Antibody, Antigen, and Control
   LSW, Anti-DNA Antibody, Antigen, and Control
   LJM, Antinuclear Antibody (Enzyme Labeled), Antigen, and Control
   MQA, Anti-Ribosomal P Antibodies
4. Panel:
   Immunology (82)

H. Intended Use:

1. Intended use(s):
   The FIDIS™ CONNECTIVE 10* kit is a semi-quantitative homogenous fluorescent-based microparticles immunoassay using flow cytometry. The test system is used to simultaneously detect the presence of 10 autoantibody specificities: double stranded DNA (dsDNA), SS-A (60kDA and TRIM 21 (52kDA)), SS-B, Sm, Sm/RNP, Scl-70, Jo-1, ribosome and centromere in human serum. *(*Antibodies to dsDNA, Sm, Sm/RNP, SS-A, SS-B, Scl-70, Jo-1, ribosomes and centromere can be reported using this assay).*
   The results of the FIDIS™ Connective 10 are to be used in conjunction with the clinical findings and the laboratory tests to aid in the diagnosis of connective diseases (systemic lupus erythematosus (SLE), Sjogrën's syndrome, mixed connective tissue disease (MCTD) scleroderma, Dermatomyositis and CREST

syndrome).
FIDIS™ Connective 10 kit uses serum only and is to be run on the FIDIS instrument and MLX-BOOSTER Software.
FIDIS™ Connective 10 kit may be used with the CARIS system (diluting and dispensing device).
This kit is for In vitro diagnostic use.

2. Indication(s) for use:
   Same as Intended use.
3. Special conditions for use statement(s):
   For prescription only.
4. Special instrument requirements:
   FIDIS™ 200 Analyzer (Luminex 200™)
   FIDIS™ MLX-Booster Software version 2.2
   FIDIS™ XY Platform
   FIDIS™ Sheath Delivery System (SD)
   Computer Central Processing Unit (PC)
   Computer Monitor Screen
   FIDIS™ Washer
   CARIS™ (Optional diluting and dispensing device)

I. Device Description:

Each device contains the following: distinct uniform size color-coded microspheres (each microsphere set is conjugated to one of the following antigens: dsDNA, SS-A 60kDA, TRIM21 (SS-A 52kDa), SS-B, Sm, Sm/RNP, Scl-70, Jo-1, ribosomes and centromere CENP-B (ready to use); calibrator (ready to use); positive control (to be diluted); negative control (to be diluted); goat anti-human IgG coupled to phycoerythrin (ready to use); sample dilution buffer (ready to use); wash buffer (ready to use); one 96 wells microplate including a filtering membrane and a lid.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   FIDIS™ Connective 10
2. Predicate K number(s):
   k071210
3. Comparison with predicate:

Similarities		
Item	New Device	Predicate Device
	FIDIS™ Connective 10	FIDIS™ Connective 10
Sample type	Serum	Same
Type of test	Semi-quantitative	Same
Platform	96 well plates	Same
Technology	Flow Cytometer based	Same
Assay Format	Multiplexed	Same
Solid-phase capture	Color-coded microspheres	Same
Conjugate	Phycoerythrin	Same
Detection method	Fluorescence	Same

Similarities		
Item	New Device	Predicate Device
Calibrator	2 wells/test	Same
Instrument	Luminometer (Luminex 200™)	Same
Software version	MLX Booster version 2.2	Same
Result Interpretation for each antibody specificity	Negative: < 30 AU/mL Borderline: 31-40 AU/mL Positive: >40 AU/mL	Same

Differences		
Item	Device	Predicate
Intended use	Individual determination of IgG antibodies to dsDNA, SS-A 60kDa, TRIM21 (SS-A 52kDa), SS-B, Sm, Sm/RNP, Scl-70, Jo-1, ribosomes and centromere (CENP-B)	Individual determination of IgG antibodies to dsDNA, SS-A 60kDA, SS-A 52, SS-B, Sm, Sm/RNP, Scl-70, Jo-1, ribosomes and centromere
New terminology of analyte name	TRIM21 (SSA 52kDa)	SSA 52kDA
Time for microspheres count	90 seconds	60 seconds
Number of counted microspheres per parameter	100 microspheres	200 microspheres

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

None provided.

L. Test Principle:

FIDIS™ Connective 10 is based on the use of distinct uniform size color-coded microspheres and a bench top 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 each specific analyte.

Each antigen required for the assay is covalently coupled to an individual set of microspheres through its surface functional groups. The different antigen coupled microspheres are mixed together, constituting the final microspheres reagent.

The test is performed in a 96 wells blank microplate including a filtering membrane at the bottom of the wells.

- In the first step, the sample is distributed in each well containing the microspheres mixture. If this sample contains one or more of the specific antibodies, they bind to the corresponding antigen(s) on one or more sets of microspheres.
- After incubation, the unbound antibodies are removed by a wash step using a filtration process.
- A phycoerythrin labeled anti-human IgG conjugate is then added that binds to the previously bound antibodies.
- A final wash step stops the reaction.
- The reaction is then directly measured by the flow cytometer, which differentiates each set of microspheres according to its fluorescence color while simultaneously measures the average fluorescence emitted by the conjugate.

A calibration system permits the determination of the antibody in AU/mL of each sample by interpolation for each antigenic specificity: SS-A 60kDa, TRIM21 (SS-A 52kDa), SS-B, Sm, Sm/RNP, Scl-70, Jo-1, ribosomes and centromere (CENP-B; and the titer in I.U/mL for the dsDNA antigenic specificity.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

For the intra-assay study, six samples for dsDNA, SS-A 60kDa, TRIM21 (SS-A 52kDa), SS-B, Sm, Sm/RNP, Jo-1, and centromere; and five samples for Scl-70 and ribosomes were analyzed 10 times (for each specificity) in one run. For the inter-assay study, the same samples were analyzed in 5 different runs. The intra-assay CV ranges for Anti-dsDNA, Anti-SS-A 60kDa & Anti-TRIM21 (SS-A 52kDa), Anti-SS-B, Anti-Sm, Anti-Sm/RNP, Anti-Scl-70, Anti-Jo-1, Anti- centromere and Anti-ribosomes were: 4-7%; 3-6%; 1-6%; 5-15%; 2-10%; 3-5%; 2-5%; 3-7%; and 3-9% respectively. The inter-assay CV ranges on Anti- dsDNA, Anti-SS-A 60kDa & Anti-TRIM21 (SS-A 52kDa), Anti-SS-B, Anti-Sm, Anti-Sm/RNP, Anti-Scl-70, Anti-Jo-1, Anti- centromere and Anti-ribosomes were: 5-10%; 4-13%; 7-14%; 6-15%; 3-15%; 6-10%; 4-11%; 4-11%; and 7-14% % respectively (see table below).

		Within-run (10 tests in the same run)		Between-run (1 test in 5 different runs)	
Antigen	Sample number	Mean value	CV (%)	Mean value	CV (%)
dsDNA	Sample 1	149	7	169	10
	Sample 2	65	5	66	5
	Sample 3	47	4	41	6
	Sample 4	42	5	45	7
	Sample 5	30	5	27	7
	Sample 6	20	4	24	10

		Within-run (10 tests in the same run)		Between-run (1 test in 5 different runs)	
Antigen	Sample number	Mean value	CV (%)	Mean value	CV (%)
SS-A 60kDa & TRIM21 (SS-A 52kDa)	Sample 7	195	3	192	5
	Sample 8	168	6	178	9
	Sample 9	75	4	67	4
	Sample 10	48	6	45	13
	Sample 11	39	4	32	10
	Sample 12	11	5	10	6
SS-B	Sample 13	96	1	98	7
	Sample 14	75	3	84	12
	Sample 15	39	4	37	13
	Sample 16	34	6	39	14
	Sample 17	23	5	27	14
	Sample 18	15	6	21	9
Sm	Sample 19	250	8	237	9
	Sample 20	103	10	92	15
	Sample 21	75	8	72	10
	Sample 22	56	5	51	9
	Sample 23	45	6	38	6
	Sample 24	29	15	29	14
Sm/RNP	Sample 25	227	10	212	8
	Sample 26	78	2	72	3
	Sample 27	62	5	57	9
	Sample 28	46	5	40	4
	Sample 29	42	4	36	12
	Sample 30	28	5	23	15
Scl-70	Sample 31	276	3	290	10
	Sample 32	119	3	127	7
	Sample 33	63	4	57	10
	Sample 34	49	5	44	8
	Sample 35	29	4	26	6
Jo-1	Sample 36	289	2	307	7
	Sample 37	64	2	74	7
	Sample 38	54	5	62	11
	Sample 39	49	5	49	4
	Sample 40	33	3	32	8
	Sample 41	22	5	22	9
Centromere	Sample 42	191	4	172	11
	Sample 43	189	3	185	9
	Sample 44	60	7	46	8
	Sample 45	51	5	56	11
	Sample 46	44	3	39	4
	Sample 47	21	7	18	15

		Within-run (10 tests in the same run)		Between-run (1 test in 5 different runs)	
Antigen	Sample number	Mean value	CV (%)	Mean value	CV (%)
Ribosome	Sample 48	312	3	312	12
	Sample 49	140	4	129	14
	Sample 50	44	6	46	10
	Sample 51	44	5	37	7
	Sample 52	31	9	30	10

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 WHO International Standard for anti-dsDNA, human code: WO/80. Other calibrators and controls (positive and negative) were prepared in-house and assigned arbitrary units per mL (AU/mL) during the development process.

d. Detection limit:
Not applicable.

e. Analytical specificity:
Interference study: Thirty samples were selected for evaluation of potential interference and crossreactivity: 2 Cryoglobulinemia, 7 Complement, 1 IgG monoclonal immunoglobulins, 5 IgM monoclonal immunoglobulins, 8 Rheumatoid Factor, 3 citrated plasmas, 2 hemolyzed samples and 1 Anti-smooth muscle antibody. Twenty six samples were negative; one of the two positive Complement sample was positive for dsDNA and other was positive for SS-A 60kDa, SS-B, Sm, and Sm/RNP; one of the two positive Rheumatoid factor sample was positive for dsDNA, SS-A 60kDa, TRIM21 (SSA 52kDa), SSB, and Sm/RNP and other was positive for SS-A 60kDa, and TRIM (SSA 52kDa). To ensure appropriate samples are used in the test, the package insert states to avoid hemolyzed, lipemic, icteric, or samples with abnormal concentration of IgG and/ or complement levels, or samples with rheumatoid factor.

f. Assay cut-off:
See Expected values/ Reference range section.

2. Comparison studies:

a. Method comparison with predicate device:
Since the modifications between the predicate and this new device were minor, a smaller sample size method comparison study was done to show the substantial equivalence of this device to the predicate device. The method comparison between the predicate and new device was performed on the same group of eighty samples for each of the ten given analytes. The positive, negative and total percent agreement for each analyte were as follows for: Anti-dsDNA: 100%, 98.4% and 98.8%; Anti-SS-A60kDa : 100%, 98.2%, and 98.8%; Anti-TRIM21 (SS-A 52kDa): 95.8%, 100%, and 98.8%; Anti-SS-B:

100%, 98.5% and 98.8%; Anti-Sm: 100%, 100% and 100%; Anti-Sm/RNP: 100%, 98.4% and 98.8%; Anti-Scl-70: 100%, 96.9% and 97.5%; Anti-Jo-1: 100%, 100% and 100%; Anti- centromere CENP-B): 100%, 98.6% and 98.8%; and Anti-ribosomes: 100%, 100% and 100%. Tabulated results are shown below. (Note: All equivocal results were considered negative)

Anti-dsDNA		FIDIS™ Connective 10		
		Positive	Negative	Total
Modified FIDIS™ Connective 10	Positive	16	1*	17
	Negative	0	63	63
	Total	16	64	80

Positive percent agreement: 100 % (16/16)
Negative percent agreement: 98.4% (63/64)
Overall percent Agreement: 98.8% (79/80)

Anti-SS-A 60kDa		FIDIS™ Connective 10		
		Positive	Negative	Total
Modified FIDIS™ Connective 10	Positive	25	1	26
	Negative	0	54	54
	Total	25	55	80

Positive percent agreement: 100 % (25/25)
Negative percent agreement: 98.2% (54/55)
Overall percent Agreement: 98.8% (79/80)

Anti-TRIM21 (SS-A 52kDa)		FIDIS™ Connective 10		
		Positive	Negative	Total
Modified FIDIS™ Connective 10	Positive	23	0	23
	Negative	1	56	57
	Total	24	56	80

Positive percent agreement: 95.8 % (23/24)
Negative percent agreement: 100% (56/56)
Overall percent Agreement: 98.8% (79/80)

Anti-SS-B		FIDIS™ Connective 10		
		Positive	Negative	Total
Modified FIDIS™ Connective 10	Positive	14	1	15
	Negative	0	65	65
	Total	14	66	80

Positive percent agreement: 100 % (14/14)
Negative percent agreement: 98.5% (65/66)
Overall percent Agreement: 98.8% (79/80)

Anti-Sm		FIDIS™ Connective 10		
		Positive	Negative	Total
Modified FIDIS™ Connective 10	Positive	17	0	17
	Negative	0	63	63
	Total	17	63	80

Positive percent agreement: 100 % (17/17)
Negative percent agreement: 100% (63/63)
Overall percent Agreement: 100% (80/80)

Anti-Sm/RNP		FIDIS™ Connective 10		
		Positive	Negative	Total
Modified FIDIS™ Connective 10	Positive	19	1	20
	Negative	0	60	60
	Total	19	61	80

Positive percent agreement: 100 % (19/19)
Negative percent agreement: 98.4% (60/61)
Overall percent Agreement: 98.8% (79/80)

Anti-Scl-70		FIDIS™ Connective 10		
		Positive	Negative	Total
Modified FIDIS™ Connective 10	Positive	15	2	17
	Negative	0	63	63
	Total	15	65	80

Positive percent agreement: 100 % (15/15)
Negative percent agreement: 96.9% (63/65)
Overall percent Agreement: 97.5% (78/80)

Anti-Jo-1		FIDIS™ Connective 10		
		Positive	Negative	Total
Modified FIDIS™ Connective 10	Positive	10	0	10
	Negative	0	70	70
	Total	10	70	80

Positive percent agreement: 100 % (10/10)
Negative percent agreement: 100% (70/70)
Overall percent Agreement: 100% (80/80)

Anti-CENP-B		FIDIS™ Connective 10		
		Positive	Negative	Total
Modified FIDIS™ Connective 10	Positive	7	1	8
	Negative	0	72	72
	Total	7	73	80

Positive percent agreement: 100 % (7/7)
Negative percent agreement: 98.6% (72/73)
Overall percent Agreement: 98.8% (79/80)

Anti-Ribosome		FIDIS™ Connective 10		
		Positive	Negative	Total
Modified FIDIS™ Connective 10	Positive	6	0	6
	Negative	0	74	74
	Total	6	74	80

Positive percent agreement: 100 % (6/6)
Negative percent agreement: 100% (74/74)
Overall percent Agreement: 99.1% (80/80)

Comparison of manual preparation and the automated CARIS™ System: The method comparison between the manual preparation and the automated CARIS™ System was performed on the same group of eighty samples for each of the ten given analytes. The positive, negative and total percent agreement for each of the analyte were as follows for Anti-dsDNA: 100%, 98.4% and 98.8%; Anti-SS-A 60kDa: 100%, 98.1%, and 98.8%; Anti-TRIM21 (SS-A 52kDa): 100%, 98.3%, and 98.8%; Anti-SS-B: 100%, 100%, and 100%; Anti-Sm: 100%, 98.4%, and 98.8%; Anti-Sm/RNP: 100%, 100%, and 100%; Anti-Scl-70: 100%, 96.9%, and 97.5%; Anti-Jo-1: 100%, 100%, 100%; Anti-centromere: 100%, 100%, and 100%; and Anti-ribosomes: 100%, 100%, and 100%. Tabulated results are shown below. (Note: All equivocal results were considered negative)

Anti-dsDNA		FIDIS™ Connective 10 Manual		
		Positive	Negative	Total
Modified FIDIS™ Connective 10 CARIS™	Positive	16	1	17
	Negative	0	63	63
	Total	16	64	80

Positive percent agreement: 100 % (16/16)
Negative percent agreement: 98.4% (63/64)
Overall percent Agreement: 98.8% (79/80)

Anti-SS-A 60kDa		FIDIS™ Connective 10 Manual		
		Positive	Negative	Total
Modified FIDIS™ Connective 10 CARIS™	Positive	26	1	27
	Negative	0	53	53
	Total	26	54	80

Positive percent agreement: 100 % (26/26)
Negative percent agreement: 98.1% (53/54)
Overall percent Agreement: 98.8% (79/80)

Anti-TRIM21 (SS-A 52kDa)		FIDIS™ Connective 10 Manual		
		Positive	Negative	Total
Modified FIDIS™ Connective 10 CARIS™	Positive	22	1	23
	Negative	0	57	57
	Total	22	58	80

Positive percent agreement: 100 % (22/22)
Negative percent agreement: 98.3% (57/58)
Overall percent Agreement: 98.8% (79/80)

Anti-SS-B		FIDIS™ Connective 10 Manual		
		Positive	Negative	Total
Modified FIDIS™ Connective 10 CARIS™	Positive	15	0	15
	Negative	0	65	65
	Total	15	65	80

Positive percent agreement: 100 % (15/15)
Negative percent agreement: 100% (65/65)
Overall percent Agreement: 100% (80/80)

Anti-Sm		FIDIS™ Connective 10 Manual		
		Positive	Negative	Total
Modified FIDIS™ Connective 10 CARIS™	Positive	16	1	17
	Negative	0	63	63
	Total	16	64	80

Positive percent agreement: 100 % (16/16)
Negative percent agreement: 98.4% (63/64)
Overall percent Agreement: 98.8% (78/80)

Anti-Sm/RNP		FIDIS™ Connective 10 Manual		
		Positive	Negative	Total
Modified FIDIS™ Connective 10 CARIS™	Positive	20	0	20
	Negative	0	60	60
	Total	20	60	80

Positive percent agreement: 100 % (20/20)
Negative percent agreement: 100% (60/60)
Overall percent Agreement: 100% (80/80)

Anti-Scl-70		FIDIS™ Connective 10 Manual		
		Positive	Negative	Total
Modified FIDIS™ Connective 10 CARIS™	Positive	15	2	17
	Negative	0	63	63
	Total	15	65	80

Positive percent agreement: 100 % (15/15)
Negative percent agreement: 96.9% (63/65)
Overall percent Agreement: 97.5% (78/80)

Anti-Jo-1		FIDIS™ Connective 10 Manual		
		Positive	Negative	Total
Modified FIDIS™ Connective 10 CARIS™	Positive	8	0	8
	Negative	0	72	72
	Total	8	72	80

Positive percent agreement: 100 % (8/8)
Negative percent agreement: 100% (72/72)
Overall percent Agreement: 100% (80/80)

Anti-CENP-B		FIDIS™ Connective 10 Manual		
		Positive	Negative	Total
Modified FIDIS™ Connective 10 CARIS™	Positive	6	0	6
	Negative	0	74	74
	Total	6	74	80

Positive percent agreement: 100 % (6/6)
Negative percent agreement: 100% (74/74)
Overall percent Agreement: 100% (80/80)

Anti-Ribosome		FIDIS™ Connective 10 Manual		
		Positive	Negative	Total
Modified FIDIS™ Connective 10 CARIS™	Positive	6	0	6
	Negative	0	74	74
	Total	6	74	80

Positive percent agreement: 100 % (6/6)
Negative percent agreement: 100% (74/74)
Overall percent Agreement: 99.1% (80/80)

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:
The reported expected ranges were estimated from 2 populations:
- 50 samples from blood donors
- 48 samples selected from their potential biological interferences and according to WHO standard for dsDNA specificity.

Arbitrary units (AU/mL)	<30 AU/mL	30-40 AU/mL	>40 AU/mL
International units (IU/mL) for Anti-dsDNA	<30 IU/mL	30-40 IU/mL	>40 IU/mL
Interpretation	Negative	Equivocal	Positive

The negative thresholds (30 AU/mL or 30 IU/mL correspond to the 97.9th percentile doe the Anti-dsDNA, Anti-SSA (60 kDa and TRIM21/ 52 kDa), Anti-Sm/RNP, 99.0% for Anti-centromere and Anti-ribosome, and 100% for Anti-SSB, Anti-Sm, Anti-Scl-70 and Anti-Jo-I for the populations studies.

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.