510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

k113863

B. Purpose for Submission:

New assay

C. Measurand:

IgG and IgA anti-deamidated gliadin peptide (DGP) antibodies

D. Type of Test:

Semi-quantitative chemiluminescent immunoassay

E. Applicant:

INOVA Diagnostics, Inc

F. Proprietary and Established Names:

QUANTA Flash™ DGP IgA
QUANTA Flash™ DGP IgG
QUANTA Flash™ DGP IgA Calibrators
QUANTA Flash™ DGP IgG Calibrators
QUANTA Flash™ DGP IgA Controls
QUANTA Flash™ DGP IgG Controls

G. Regulatory Information:

1. Regulation section:

   21 CFR §866.5750 – Radioallergosorbent (RAST) Immunological Test System
   21 CFR §862.1150 – Calibrator
   21 CFR §862.1660 – Quality Control Material (Assayed and Unassayed)

2. Classification:

   Class II (Assay and calibrator)
   Class I (Control)

3. Product code:

   MST – Antibodies, Gliadin
   JIX – Calibrator, Multi-Analyte Mixture
   JJX – Single (Specified) Analyte Controls (Assayed and Unassayed)

4. Panel:

   Immunology (82)
   Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   The QUANTA Flash™ DGP IgA is a chemiluminescent immunoassay for the semi-quantitative determination of IgA antibodies to synthetic, deamidated gliadin peptides in human serum. The presence of IgA deamidated gliadin peptides antibodies can be used in conjunction with clinical findings and other laboratory tests to aid in the diagnosis of celiac disease and dermatitis herpetiformis.

   The QUANTA Flash™ DGP IgG is a chemiluminescent immunoassay for the semi-quantitative detection of IgG antibodies to synthetic, deamidated gliadin peptides in human serum. The presence of IgG deamidated gliadin peptide antibodies can be used in conjunction with clinical findings and other laboratory tests to aid in the diagnosis of celiac disease in both IgA sufficient and IgA deficient subjects, as well as dermatitis herpetiformis.

   The QUANTA Flash™ DGP IgA Calibrators are intended for use with the QUANTA Flash™ DGP IgA chemiluminescent immunoassay to establish points of reference for the working curve that is used to determine Chemiluminescent Unit (CU) values in the measurement of IgA anti-DGP antibodies in serum.

   The QUANTA Flash™ DGP IgG Calibrators are intended for use with the QUANTA Flash™ DGP IgG chemiluminescent immunoassay to establish points of reference for the working curve that is used to determine Chemiluminescent Unit (CU) values in the measurement of IgG anti-DGP antibodies in serum.

   The QUANTA Flash DGP IgA Controls are intended for quality control purposes of the QUANTA Flash DGP IgA chemiluminescent immunoassay (CIA) kit run on the BIO FLASH ® Instrument that is used for the measurement of IgA anti-deamidated gliadin peptide (DGP) antibodies in human serum.

   The QUANTA Flash DGP IgG Controls are intended for quality control purposes of the QUANTA Flash DGP IgG chemiluminescent immunoassay (CIA) kit run on the BIO FLASH ® Instrument that is used for the measurement of IgG anti-deamidated gliadin

peptide (DGP) antibodies in human serum.

2. Indication(s) for use:

   Same as Intended Use

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   BIO-FLASH™ Instrument System (k083518)

I. Device Description:

The QUANTA Flash™ DGP IgA and IgG reagent cartridges contain the following reagents:

- DGP coated paramagnetic beads in buffer, containing protein stabilizers and preservative.
- Assay buffer – containing Tris-buffered saline, Tween 20, protein stabilizers and preservatives.
- Tracer IgA or IgG – Isoluminol labeled anti-human IgA or IgG antibodies in buffer, containing protein stabilizers and preservative.

The QUANTA Flash™ DGP IgA or IgG Calibrators set includes two calibrators (Calibrator 1 and Calibrator 2). These are barcoded tubes containing 0.3 mL pre-diluted, ready-to-use reagent. Calibrators contain human IgA or human IgG antibodies to DGP in buffer. The calibration process utilizes the 2 calibrators included in the Calibrators set to adjust the predefined master curve into an instrument specific working curve. This working curve is used to calculate chemiluminescent unit (CU) values from the measured relative light units (RLU). The working curve is lot-specific, and is stored in the system for use with any reagent pack from that lot.

The QUANTA Flash™ DGP IgA or IgG Controls contain four vials (two each of Negative and Positive Controls) containing human antibodies to DGP in buffer, protein stabilizers and preservatives.

J. Substantial Equivalence Information:

1. Predicate device name(s) and Predicate 510(k) number(s):

   QUANTA Lite™ Gliadin IgA II, k052143
   QUANTA Lite™ Gliadin IgG II, k052142

2. Comparison with predicate:

Similarities		
Item	Device QUANTA Flash™ DGP IgA/IgG	Predicate QUANTA Lite™ Gliadin IgA/IgG II
Intended Use	Semi-quantitative determination of IgA/IgG antibodies to synthetic, deamidated gliadin peptides in human serum.	Same
Assay methodology	Solid phase (heterogeneous) immunoassay	Same
Antigen	Synthetic, deamidated gliadin peptides	Same
Assay Type	Semi-quantitative immunoassay	Same
Sample matrix	Serum	Same
Shelf life	One year	Same

Differences		
Item	Device QUANTA Flash™ DGP IgA/IgG	Predicate QUANTA Lite™ Gliadin IgA/IgG II
Detection/ Operating principle	Chemiluminescent immunoassay (CIA) using paramagnetic microparticles (beads)	Enzyme-linked immunosorbent assay (ELISA)
Conjugate	Isoluminol conjugated anti-human IgA/IgG	Horse radish peroxidase (HRP)-conjugated goat anti-human IgA/IgG
Signal Detected	Luminescence (visible light)	Absorbance at 450nm
Calibration	Lot specific Master Curve + two calibrators (Sold separately)	Gliadin IgA/IgG II ELISA Low Positive and High Positive (Included in the kit)

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

CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition

CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

CLSI EP7-A2: Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition

CLSI EP9-A2 IR: Method Comparison and Bias Estimation Using Patient samples; Approved Guideline – Second Edition (Interim Revision)

CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline

CLSI C28-A3c: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition

L. Test Principle:

Anti-DGP antibodies present in the serum bind to DGP-coated paramagnetic beads during an incubation step. The unbound sample is washed away and isoluminol conjugated anti-human IgA (or IgG) antibody is added. After washing away any unbound conjugate, the remaining isoluminol conjugate bound to the DGP-coated paramagnetic beads is exposed to a catalyst and an oxidizing agent. The light produced from this reaction is measured as relative light units (RLU) by the BIO-FLASH optical system. The RLU are proportional to the amount of bound isoluminol conjugate, which in turn is proportional to the amount of anti-DGP antibodies bound to the DGP on the beads.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility studies:

      i) *Reproducibility:* QUANTA Flash™ DGP IgA and IgG assays reproducibility testing was performed in accordance with CLSI EP5-A2 Guideline, at three different testing sites (one internal and two externals sites) using three specimens including one negative, one around-the-cutoff low positive and one medium positive. Samples were run in duplicates four times a day for 10 days, resulting in 80 individual data points. Two reagent lots, two calibrator lots and two operators were included as variables at the internal site. Total coefficient of variation (CV) was calculated based on within-run, between-run, between-reagent-lots, between-calibrator-lots, between-operators and between-sites precision.

QUANTA Flash™ DGP IgA:

Sample	Mean (CU)	Within Run CV%	Between Run CV%	Between Reagent Lots CV%	Between Calibrator Lots CV%	Between Operators CV%	Between Sites CV%	Total CV%
1	12.9	6.4	5.2	3.1	5.6	5.8	9.1	14.8
2	25.5	3.8	5.5	4.1	6.3	2.3	7.0	12.6
3	136.8	2.9	6.5	5.5	7.6	3.2	8.3	14.7

QUANTA Flash™ DGP IgG:

Sample	Mean (CU)	Within Run CV%	Between Run CV%	Between Reagent Lots CV%	Between Calibrator Lots CV%	Between Operators CV%	Between Sites CV%	Total CV%
1	13.4	2.6	5.9	4.0	7.5	3.6	8.1	13.5
2	21.0	2.3	5.5	3.5	7.3	4.0	7.6	12.9
3	118.9	2.4	4.9	2.3	2.3	4.0	8.1	10.9

ii) *Within-Laboratory Precision*: The within laboratory precision of the QUANTA Flash™ DGP IgA and IgG assays was evaluated in accordance with CLSI EP5-A2 Guideline.

Eight samples each representing entire reportable range of DGP IgA or DGP IgG antibodies and with samples close to the cutoff were run in duplicates, twice a day, for at least 20 days resulting in ≥80 individual data points. Data were analyzed and within-run, between-run, between-day and total precisions are summarized in the Table below.

QUANTA Flash™ DGP IgA:

Sample	Mean (CU)	Within-Run CV%	Between-Run CV%	Between-Day CV%	Total CV%
1	10.5	4.0%	1.9%	5.8%	7.3%
2	15.4	5.8%	0.0%	6.2%	8.5%
3	32.4	3.1%	0.8%	6.8%	7.5%
4	33.0	4.1%	0.0%	8.8%	9.7%
5	35.1	5.9%	0.0%	10.7%	12.2%
6	105.6	5.1%	0.0%	6.4%	8.2%
7	128.8	4.6%	3.2%	6.7%	8.7%
8	1930.8	4.9%	3.3%	7.8%	9.8%

QUANTA Flash™ DGP IgG:

Sample	Mean (CU)	Within-Run CV%	Between-Run CV%	Between-Day CV%	Total CV%
1	5.8	3.1%	2.5%	2.0%	4.5%
2	16.8	3.0%	0.5%	1.5%	3.3%
3	20.7	2.5%	1.3%	2.2%	3.6%
4	24.6	1.9%	1.8%	1.5%	3.0%
5	85.1	2.2%	0.9%	2.9%	3.8%
6	411.6	1.9%	1.6%	2.3%	3.4%
7	791.0	3.1%	2.0%	0.7%	3.8%
8	1781.4	2.9%	1.6%	2.7%	4.3%

b. Linearity/assay reportable range:

i) *Linearity*: The QUANTA Flash™ DGP IgA and IgG assay linearity studies were evaluated in accordance with CLSI EP6-A Guideline. In each assay, six serum samples with various DGP IgA (or IgG) concentrations were diluted with a low negative serum to obtain values that cover the whole analytical measuring range (AMR). The observed values were graphed against the calculated values and linear regression was performed. The study results are summarized in the table below:

The QUANTA Flash™ DGP IgA:

Sample	Test Range (CU)	Slope (95% CI)	Y-intercept (95% CI)	R^2
1	5.2 to 34.0	1.00 (0.9 to 1.1)	0.61 (-1.3 to 2.5)	0.99
2	7.6 to 128.7	1.01 (1.0 to 1.0)	-0.17 (-2.3 to 2.0)	1.00
3	5.2 to 356.5	1.02 (1.0 to 1.1)	4.24 (-4.0 to 12.5)	0.99
4	5.2 to 748.1	1.02 (1.0 to 1.0)	3.32 (-2.1 to 8.7)	1.00
5	96.7 to1990.4	1.02 (1.0 to 1.1)	10.46 (-24.3 to 45.2)	1.00
6	91.5 to 2596.8	0.96 (0.9 to 1.1)	-69.15 (-204.5 to 66.2)	0.99

The claimed reportable Analytical Measuring range is 5.2 CU – 2,367.3 CU.

QUANTA Flash™ DGP IgG:

Sample	Test Range (CU)	Slope (95% CI)	Y-intercept (95% CI)	R^2
1	1.9 to 36	1.06 (1.0 to 1.1)	-2.37 (-3.1 to -1.7)	1.00
2	6.8 to 81.9	0.97 (0.9 to 1.0)	0.04 (-2.0 to 2.1)	0.99
3	18.6 to 173.6	1.04 (1.0 to 1.1)	5.46 (-1.1 to 12.0)	0.99
4	39.6 to 449.8	0.94 (0.9 to 1.0)	-2.06 (-16.0 to 11.9)	0.99
5	213.2 to 1,668	0.95 (0.9 to 1.0)	101.97 (72.2 to 131.7)	1.00
6	255.8 to 2,565.4	0.99 (0.9 to 1.0)	79.28 (-4.0 to 162.6)	0.99

The claimed reportable Analytical Measuring range is 2.8 CU – 1,936.7 CU.

ii) *Dilution Recovery*: The BIO-FLASH software has an Auto-rerun option available. If this option is selected, the instrument will automatically rerun any sample that has a result >2,367.3 CU for DGP IgA or >1,936.7 for DGP IgG, by further diluting it by a factor of 10, and calculating the actual CU using this additional dilution factor.

To confirm the Auto-rerun function, two high positive specimens with results above the analytical measuring range were selected for each assay. The samples were run with the Auto-rerun function enabled on the BIO-FLASH. Then the specimens were manually diluted the same way as it happens in the Auto-rerun function (10 fold dilution), and tested on the BIO-FLASH. The results were within the analytical measuring range after auto-rerun or manual dilution for all specimens. The differences between the manual and automatic results for DGP IgA were 11% and 15%, and for the DGP IgG 19% and 5%.

iii) *High Concentration Hook-effect*: To assess hook effect, the measurement signal (i.e., RLU) was examined for high positive specimens with results above the analytical measuring range before and after automatic or manual dilution. All sera produced significantly higher RLU values when used "as is" compared to the manually or automatically diluted ones, thereby confirming that high positive specimens above the analytical measuring range do not show hook effect up to 5167.2 CU in the DGP IgA assay and up to 4323.7 CU in the DGP IgG assay.

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

i) *Traceability*: There is currently no recognized international standard for the measurement of IgA or IgG anti-deamidated gliadin peptide antibodies. Calibrators are assigned values based on a 20 unit cutoff between positive and negative during assay development.

ii) *Calibrator and controls:*

Calibrators: The QUANTA Flash™ DGP IgA (or IgG) chemiluminescent immunoassay utilizes predefined lot specific master curve that is stored in the reagent cartridge barcode. The QUANTA Flash™ DGP IgA (or IgG) Calibrators are designed to produce an instrument specific working curve from the parameters of the master curve, with a decision point based on the performance characteristics and clinical evaluation of the QUANTA Flash™ DGP IgA (or IgG) assay. Calibrators are tested on multiple instruments with multiple lots of reagents prior to value assignment.

Stability studies demonstrated that both the QUANTA Flash™ DGP IgA and IgG Calibrators can be used for up to 4 calibrations over an 8 hour period.

Controls: The QUANTA Flash™ DGP IgA (or IgG) Controls are made up of a Negative Control and a Positive Control. Each contains a different amount of IgA (or IgG) anti-DGP antibodies. The Negative Control is designed to assess precision and accuracy of the assay at very low antibody levels. The Positive Control is designed to assess precision and accuracy of the assay at moderate to high antibody levels.

Stability studies demonstrated that opened Controls can be used for up to 15 times, with a maximum time of 10 minutes onboard the instrument per use. The total time the control tubes can be uncapped onboard the instrument is 2½ hours, or 10 minutes per use.

iii) *Kit Stability*: Stability studies support that the QUANTA Flash™ DGP IgA reagent cartridge in-use (on-board) stability is 40 days, and the QUANTA Flash™ DGP IgG reagent cartridge in-use (on-board) stability is 62 days. Accelerated stability studies also support that the QUANTA Flash™ DGP IgA and IgG assays, as well as the Calibrators and Controls have a shelf life of one year at 2-8^{o}C.

d. Detection limit:

QUANTA Flash™ DGP IgA: The Limit of Detection (LoD) of the QUANTA Flash™ DGP IgA assay is 730.3 RLU or 1.826 chemiluminescent unit (CU), which is below the analytical measuring range of the assay. It was determined consistent with CLSI EP17-A guideline with proportions of false positives (alpha) less than 5% and false negatives (beta) less than 5%; based on 140 determinations, with 60 blank and 80 low level samples. The LoB is 504.9 RLU or 1.262 CU.

QUANTA Flash™ DGP IgG: The Limit of Detection (LoD) of the QUANTA Flash™ DGP IgG assay is 469.2 RLU or 0.626 CU, which is below the analytical measuring range of the assay. It was determined consistent with CLSI EP17-A guideline with proportions of false positives (alpha) less than 5% and false negatives (beta) less than 5%; based on 140 determinations, with 60 blank and 80 low level samples. The LoB is 257.7 RLU or 0.344 CU.

e. Analytical specificity:

i) *Cross-reactivity*:

QUANTA Flash™ DGP IgA: To test potential cross-reactivity with autoantibodies and infection-induced antibodies, 201 patient samples were tested from patients with infectious diseases, autoimmune diseases and connective tissue diseases, including those characterized with gastrointestinal symptoms. None of those specimens were positive in the QUANTA Flash™ DGP IgA test.

QUANTA Flash™ DGP IgG: To test potential cross-reactivity with autoantibodies and infection-induced antibodies, 185 patient samples were tested from patients with infectious diseases, autoimmune diseases and connective tissue diseases, including those characterized with gastrointestinal symptoms. Two out of the 31 viral hepatitis specimens, two out of the 17 *H. pylori* infection specimens, and one out of the 37 rheumatoid arthritis specimens were positive with the QUANTA Flash™ DGP IgG assay. Altogether, only five out of the 185 specimens (3%) were positive, indicating the minimal cross-reactivity.

ii) *Interference*: The interference study was performed according to CLSI EP07-A2 Guideline.

QUANTA Flash™ DGP IgA: Three specimens, including one negative (5.8 CU), one around-the-cutoff low positive (24.7 CU) and one medium positive (186.9 CU), were tested. Interfering substances were spiked into every specimen at three different concentrations in 10% of total specimen volume, and the resulting samples were analyzed in triplicates with the DGP IgA assay. Recovery of the unit values was calculated compared to control samples spiked with the same volume of diluents. No interference was detected with bilirubin up to 10 mg/dL, hemoglobin up to 200 mg/dL, triglycerides up to 1,000 mg/dL, cholesterol up to 224.3 mg/dL and with rheumatoid factor IgM up to 500 IU/mL.

QUANTA Flash™ DGP IgG: Four specimens, including one negative (12.8 CU), two around-the-cutoff low positive (32 and 41.3 CU) and one medium positive (139.8 CU), were tested. Interfering substances were spiked into every specimen at three different concentrations in 10% of total specimen volume, and the resulting samples were analyzed in triplicates with the QUANTA Flash™ DGP IgG assay. Recovery of the unit values was calculated compared to control samples spiked with the same volume of diluents. No interference was detected with bilirubin up to 10 mg/dL, hemoglobin up to 200 mg/dL, triglycerides up to 1000 mg/dL or·cholesterol up to 224.3 mg/dL and rheumatoid factor lgM up to 500 IU/mL.

f. Assay cut-off: The cut off was established in accordance to CLSI C28-A3c Guideline.

QUANTA Flash™ DGP IgA: The assay cutoff of 20 CU was determined by testing 355 serum samples from control population including 201 healthy subjects.

QUANTA Flash™ DGP IgG: The assay cutoff of 20 CU was determined by testing 292 serum samples from control population including 201 healthy subjects.

2. Comparison studies:

a. Method comparison with predicate device:

QUANTA Flash™ DGP IgA: One hundred and two samples within the reportable range of the assay were tested with the QUANTA Flash™ DGP IgA assay and the predicate method. The samples were collected from normal subjects, diagnosed celiac (CD) patients, and patients with other defined diseases non-CD and dermatitis herpetiformis (DH) patients. These samples were tested on both the QUANTA Flash™ DGP IgA CIA and on the predicate ELISA. The study results are summarized in the table below.

		QUANTA Lite™ Gliadin IgA II		
		Positive	Negative	Total
QUANTA Flash™ DGP IgA	Positive	65	3*	68
	Negative	6**	28	34
	Total	71	31	102

(*) Two patients were suspected CD with no diagnosis, while the third was a DH patient. (**) Two patients had DH. Three patients had CD, two without clinical presentation, one with a Marsh III biopsy. The last patient had ulcerative colitis

Positive Agreement = 91.5% (95% C.I. = 82.5 – 96.8%)
Neg. Agreement = 90.3% (95% C.I. = 74.2 – 98.0%)
Overall Agreement = 91.2% (95% C.I. = 83.9 – 95.9%)

In separate analyses, 21 samples from patients with DH were compared to the predicate. The study results are summarized in the tables below.

		QUANTA Lite™ Gliadin IgA II		
		Positive	Negative	Total
QUANTA Flash™ DGP IgA	Positive	12	1	13
	Negative	2	6	8
	Total	14	7	21

Positive Agreement = 85.7% (95% C.I. = 57.2% – 98.2%)
Negative Agreement = 85.7% (95% C.I. = 42.1 – 99.6%)
Overall Agreement = 85.7% (95% C.I. = 63.7% – 97.0%)

QUANTA Flash™ DGP IgG: Two hundred and forty one samples within the reportable range of the assay were tested with the QUANTA Flash™ DGP IgG assay and the predicate method.

The samples were collected from normal subjects, diagnosed celiac (CD) patients, and patients with other defined diseases non-CD and DH patients. These samples were tested on both the QUANTA Flash™ DGP IgG CIA and on the predicate ELISA. The study results are summarized in the table below.

		QUANTA Lite™ Gliadin IgG II		
		Positive	Negative	Total
QUANTA Flash™ DGP IgG	Positive	78	26*	104
	Negative	4**	133	137
	Total	82	159	241

(*) Thirteen samples were from CD patients; three being on gluten-free diet. One sample was from a suspected CD patient that is IgA anti-DGP positive. Two samples had H. pylori gastritis, two had viral hepatitis, and one had rheumatoid arthritis. One patient, with low blood count, was IgG anti-h-tTG positive. The remaining 6 samples were from apparently healthy individuals; one had gastrointestinal symptoms at time of sample collection, with two being IgA anti-h-tTG positive. (**) Three samples were from CD patients, and one was from a DH patient.

Positive Agreement = 95.1% (95% C.I. = 88.0 – 98.7%)
Negative Agreement = 83.6% (95% C.I. = 77.0 – 89.0%)
Overall Agreement = 87.6% (95% C.I. = 82.7 – 91.4%)

In separate analyses, the results of thirteen IgA deficient samples from patients with diagnosed celiac disease were compared to the predicate, and 23 samples from patients with DH were compared to the predicate. The study results are summarized in the tables below.

IgA Deficient Celiac Disease:

		QUANTA Lite™ Gliadin IgG II		
		Positive	Negative	Total
QUANTA Flash™ DGP IgG	Positive	5	2	7
	Negative	2	4	6
	Total	7	6	13

Positive Agreement = 71.4% (95% C.I. = 29.0% – 96.3%)
Negative Agreement = 66.7% (95% C.I. = 22.3% – 95.7%)
Overall Agreement = 69.2% (95% C.I. = 38.6% – 90.9%)

Dermatitis Herpetiformis:

		QUANTA Lite™ Gliadin IgG II		
		Positive	Negative	Total
QUANTA Flash™ DGP IgG	Positive	16	0	16
	Negative	2	5	7
	Total	18	5	23

Positive Agreement = 88.9% (95% C.I. = 65.3% – 98.6%)

Negative Agreement = 100.0% (95% C.I. = 47.8% – 100.0%)
Overall Agreement = 91.3% (95% C.I. = 72.0% – 98.9%)

b. Matrix comparison:

Not applicable.

3. Clinical studies:

a. Clinical Sensitivity and Specificity:

QUANTA Flash™ DGP IgA: The clinical validation study included 54 CD samples (39 samples from patients with CD but on gluten free diet or with unconfirmed CD), 103 non-celiac disease controls, and 21 samples from patients with DH. A separate external study included 93 CD samples, 151 samples from individuals seeking medical attention in whom CD was excluded based on physical exam and diagnostic tests, and 98 disease controls. The results were analyzed to calculate sensitivity and specificity for CD (n=147) and DH (n=21) separately using the same control population (n=352). The results of this testing are shown in the Tables below:

Clinical sensitivity and specificity of the QUANTA Flash™ DGP IgA assay in CD (total population):

		Diagnosis		
		CD	Not CD	Total
QUANTA Flash™ DGP IgA	Positive	105	0	105
	Negative	42	352	394
	Total	147	352	499

Sensitivity = 71.4% (95% C.I. = 63.4 – 78.6%)
Specificity = 100.0% (95% C.I. = 99.0 – 100%)

The distribution and positivity rate in the disease control population:

Patient Group	N	# of positives
Autoimmune liver disease	5	0
Viral hepatitis	47	0
Inflammatory bowel disease (Crohn's Disease and Ulcerative Colitis)	17	0
H. pylori infection	17	0
Food allergy	9	0
Systemic rheumatic disease	12	0
Autoimmune thyroid disease	22	0
Patients with gastrointestinal symptoms	11	0
Type 1 diabetes mellitus	14	0

Rheumatoid arthritis	37	0
Other infectious disease (HIV, Syphilis)	10	0
Total	201	0

Diagnostic sensitivity and specificity were calculated on the DH group separately, and the results are shown in the Table below.

Clinical sensitivity and specificity of the QUANTA Flash™ DGP IgA assay in DH:

		Diagnosis		
		DH	Not DH	Total
QUANTA Flash™ DGP IgA	Positive	13	0	13
	Negative	8	352	360
	Total	21	352	373

Sensitivity = 61.9% (95% C.I. = 38.4 – 81.9%)
Specificity = 100.0% (95% C.I. = 99.0 – 100%)

QUANTA Flash™ DGP IgG: The clinical validation study included 62 CD samples from INOVA's serum library (including 7 with selective IgA deficiency), 87 non-celiac disease controls, 39 samples from patients with CD but on gluten free diet or with unconfirmed CD, and 23 samples from patients with DH. A separate external study included 102 CD samples (including 9 with selective IgA deficiency), 151 samples from individuals seeking medical attention in whom CD was excluded after physical exam and diagnostic tests, and 98 disease controls. The results were analyzed to calculate sensitivity and specificity for CD (n=148) and DH (n=23) separately using the same control population (n=336).

Clinical sensitivity and specificity of the QUANTA Flash™ DGP IgG assay in CD (total population):

		Diagnosis		
		CD	Not CD	Total
QUANTA Flash™ DGP IgG	Positive	132	9*	141
	Negative	16	327	343
	Total	148	336	484

(*) Two samples had H. pylori gastritis, two had viral hepatitis, and one had rheumatoid arthritis.

Sensitivity = 89.2% (95% C.I. = 83.0 – 93.7%)
Specificity = 97.3% (95% C.I. = 95.0 – 98.8%)

The distribution and positivity rate in the disease control population:

Patient Group	n	# of positives
Autoimmune liver disease	5	0
Viral hepatitis	31	2
Inflammatory bowel disease (Crohn's Disease and Ulcerative Colitis)	17	0
H pylori infection	17	2
Food allergy	9	0
Systemic rheumatic disease	12	0
Autoimmune thyroid disease	22	0
Patients with gastrointestinal symptoms	11	0
Type 1 diabetes mellitus	14	0
Rheumatoid arthritis	37	1
Other infectious disease (HIV, Syphilis)	10	0
Total	185	5

Altogether 16 samples were from IgA deficient CD patients. Nine out of 16 (56.3%) were positive with the QUANTA Flash™ DGP IgG assay, indicating that the assay is a useful tool for CD screening in IgA deficient subjects.

Clinical sensitivity and specificity of the QUANTA Flash™ DGP IgG assay in IgA deficient CD:

		Diagnosis		
		CD (IgA deficient)	Not CD	Total
QUANTA Flash™ DGP IgG	Positive	9	9	18
	Negative	7	327	334
	Total	16	336	352

Sensitivity = 56.3% (95% C.I. = 29.9 – 80.2%)
Specificity = 97.3% (95% C.I. = 95.0 – 98.8%)

Diagnostic sensitivity and specificity were calculated on the DH group separately, and the results are shown in the Table below.

Clinical sensitivity and specificity of the QUANTA Flash™ DGP IgG assay in DH:

		Diagnosis		
		DH	Not DH	Total
QUANTA Flash™ DGP IgG	Positive	16	9*	25
	Negative	7	327	334
	Total	23	336	359

(*)Two samples have H. pylori gastritis, two have viral hepatitis, and one has rheumatoid arthritis.

Sensitivity = 69.6% (95% C.I. = 47.1 – 86.8%)
Specificity = 97.3% (95% C.I. = 95.0 – 98.8%)

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

Not applicable

4. Clinical cut-off**:**

See Assay Cutoff above.

5. Expected values/Reference range:

QUANTA Flash™ DGP IgA: The expected result in the normal population is "negative". The prevalence of CD in the not-at-risk reference population is close to 1%, so occasional positive results can be expected when healthy subjects are tested. A study of 232 apparently healthy individuals tested with the QUANTA Flash™ DGP IgA assay showed that ~1% were positive (one positive and one weak positive).

QUANTA Flash™ DGP IgG: The expected result in the normal population is "negative". The prevalence of CD in the not-at-risk reference population is close to 1%, so occasional positive results can be expected when healthy subjects are tested. A study of 232 apparently healthy individuals tested with the QUANTA Flash DGP™ IgG assay showed that ~2% were positive (four positive and one weak positive).

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.