

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

A. 510(k) Number:

k081248

B. Purpose for Submission:

New Device

C. Measurand:

Anti-OMP IgA Antibodies

D. Type of Test:

Semi-quantitative ELISA

E. Applicant:

INOVA Diagnostics, Inc.

F. Proprietary and Established Names:

QUANTA Lite™ OMP Plus IgA ELISA

G. Regulatory Information:

1. Regulation section:

21 CFR 866.5785 - Anti-Saccharomyces cerevisiae (*S. Cerevisiae*) Antibody (ASCA) Test Systems.

2. Classification:

Class II

3. Product code:

OKM, Antibodies, outer-membrane proteins

4. Panel:

Immunology 82

H. Intended Use:

1. Intended use(s):

The QUANTA Lite™ OMP Plus kit is an enzyme-linked immunosorbent assay (ELISA) for the semi-quantitative detection of anti-OMP antibodies of the IgA class in human serum. It is intended to be used in conjunction with anti-*Saccharomyces cerevisiae* (*S. cerevisiae*) antibody (ASCA) IgG and/or IgA test systems. The presence of OMP (outer membrane proteins) IgA antibodies, used in conjunction with clinical findings and other laboratory tests, may aid in the diagnosis of patients with Crohn's disease.

2. Indication(s) for use:

Same as Intended Use.

3. Special conditions for use statement(s):

Prescription use only.

4. Special instrument requirements:

Microplate reader capable of measuring OD at 450 nm (or 620 for dual wavelength readings)

I. Device Description:

QUANTA Lite™ OMP Plus ELISA consists of a polystyrene microwell ELISA plate coated with a proprietary lysate of outer membrane and associated proteins derived from 2 strains of anaerobic bacteria; high positive, low positive, and negative controls; sample diluent; wash concentrate; goat anti-human IgG horseradish peroxidase

conjugate; TMB chromogen; and stop solution.

J. Substantial Equivalence Information:

1. Predicate device name(s):
QUANTA Lite™ ASCA IgG ELISA
2. Predicate K number(s):
k000732
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Indication for Use	To aid in the diagnosis of patients with Crohn's disease.	Same
Technology	ELISA	Same
Assay Format	Semi-quantitative	Same
Platform	96 well microtiter plates	Same
ELISA Negative control	Pre-diluted human serum, Ready to use	Same
Sample type and dilution	Serum, 1:101	Same
Sample volume	5 uL	Same
Enzyme conjugate	Horseradish peroxidase, goat anti-human IgG	Same
Substrate	TMB Chromogen	Same
Incubation times	30-30-30 minutes	Same
O.D. Reading	450 nm (or 620 for dual wavelength readings)	Same
Result Interpretation	<20 units = negative 20–24.9 units = equivocal ≥ 25 units = positive	Same
Cut-off	25	Same

Differences		
Item	Device	Predicate
Intended Use	Semi-quantitative detection of anti-OMP (outer membrane proteins) antibodies of the IgA class in human serum. To be used in conjunction with ASCA (IgG and IgA).	Semi-quantitative detection of anti- <i>Saccharomyces cerevisiae</i> antibodies (ASCA) of the IgG class in human serum.
Antigen	Partially purified lysate of outer membrane and associated proteins from two different species of intestinal bacteria	Partially purified and disrupted <i>S.cerevisiae</i> antigen
High Positive and Low Positive Controls	OMP Plus IgA ELISA High and Low positive controls. Pre-diluted. Ready to use	ASCA IgG ELISA High and Low positive controls. Pre-diluted. Ready to use

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

Not referenced.

L. Test Principle:

A proprietary lysate of partially purified outer membrane and associated proteins derived from 2 species of anaerobic bacteria are bound to the wells of a polystyrene microwell plate under conditions that will preserve the antigen in its native state. Pre-diluted controls and diluted patient sera are added to separate wells, allowing any OMP antibodies present to bind to the immobilized antigen. Unbound sample is washed away and an enzyme labeled anti-human IgA conjugate is added to each well. A second incubation allows the enzyme labeled anti-human IgA to bind to any patient antibodies, which have become attached to the microwells. After washing away any unbound enzyme labeled anti-human IgA, the remaining enzyme activity is measured by adding a chromogenic substrate and measuring the intensity of the color that develops. The assay can be evaluated spectrophotometrically by measuring and comparing the color intensity that develops in the patient wells with the color in the control wells.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Intra-assay studies: Eight samples (3 specimens with moderate OMP antibody levels (46.2, 45.5, 41.8 units, respectively), 2 specimens just over the cut-off (26.9, 26.3 units, respectively), and 3 equivocal samples (21.8, 23.9, 24.5 units, respectively)) were assayed in 10 replicates each. Results showed acceptable %CV ranging from 2.1 to 6.4.

Intra-assay Performance of QUANTA Lite™ OMP Plus ELISA

	Specimen							
	1	2	3	4	5	6	7	8
Mean units	46.2	26.9	45.5	26.3	41.8	24.5	23.9	21.8
SD	1.17	0.78	2.91	0.72	0.93	0.86	0.83	0.46
CV %	2.5	2.9	6.4	2.8	2.2	3.5	3.5	2.1

Inter-assay: Nine specimens (2 equivocal, 3 low positive, and 3 moderate positive) plus the high positive control were tested in duplicate twice daily for 3 days. The results showed acceptable %CV ranging from 1.1 to 4.3.

Inter-assay Performance for QUANTA Lite™ OMP Plus ELISA

	Specimen								
	HPC	1	2	3	4	5	6	7	8
Mean units	69.8	50.0	26.6	54.1	29.2	46.2	27.3	24.7	23.5
SD	2.35	0.74	0.89	2.23	1.07	1.63	1.14	1.07	0.89
CV %	3.4	1.1	3.4	4.1	3.7	3.5	4.2	4.3	3.8

b. *Linearity/assay reportable range:*

No claims were made regarding linearity for the assay. Reactivity is related to the quantity of antibody present in a non-linear fashion.

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

There is no reference standard for OMP Antibodies. The results are reported in arbitrary units

d. *Detection limit:*

Not applicable.

e. *Analytical specificity:*

Interference:

Interference by endogenous substances: No data provided. The package insert states that grossly hemolyzed, icteric, microbially contaminated, or heat-treated samples should be avoided in this assay.

Cross-reactivity with other autoantibodies:

Sera from 36 patients with various autoimmune or infectious disease and positive for associated antibodies including 8 rheumatoid arthritis, 2 soluble liver antigen (SLA), 2 liver kidney microsome (LKM), 2 chromatin, 2 Jo-1, 2 centromere, 1 SS-A, 2 SS-B, 2 anti-mitochondrial antibody (AMA), 2 tissue transglutaminase (tTG), 1 Scl-10, 1 RNP, 3 glomerular basement membrane (GBM), 2 cytomegalovirus (CMV), 2 rubella virus, 2 herpes simplex virus (HSV), were tested with the QUANTA Lite™ OMP Plus ELISA to assess the assay's specificity. No specimens were interpreted as positive and only one sample (an autoimmune hepatitis patient positive for SLA) was interpreted as equivocal at 22.2 units on the OMP Plus ELISA. Additional testing showed the specimen was moderately positive for ASCA IgG (76.1 units) and had an equivocal level of ASCA IgA antibodies. Sera from 226 patients with celiac disease were tested with the OMP Plus IgA ELISA and 27% were found positive. On the same cohort, 27% were positive for ASCA IgA and 31% for ASCA IgG antibodies. 14 (6.2%) of the celiac patients were triple positive (OMP Plus IgA, ASCA IgG, and ASCA IgA).

f. *Assay cut-off:*

To validate the cut-off, a panel of 500 apparently healthy individuals from the US (250 male and 250 female) with a median age of 41 years (range 18-80 years old) were tested. The median value obtained was 12.5 units. The cutoff was set at 25 units. This resulted in a specificity of 92% (468/500).

2. Comparison studies:

a. *Method comparison with predicate device:*

A panel of 1186 sera consisting of 365 specimens from patients with Crohn's disease (CD) and 821 patients from patients without Crohn's disease including specimens from 234 patients with ulcerative colitis (UC) and 587 healthy controls were tested with both the QUANTA Lite™ OMP Plus ELISA and the predicate QUANTA Lite™ ASCA IgG ELISA. Demographic information for the patient population was not available. The CD, UC and normal samples for the clinical method comparison were of European and Canadian origin.

		QUANTA Lite™ ASCA IgG ELISA			
		Pos	Eq*	Neg	Total
QUANTA Lite™ OMP Plus ELISA	Pos	117	13	70	200
	Eq*	34	14	52	100
	Neg	167	45	674	886
	Total	318	72	796	1186

*Equivocal results counted as negative (not-positive).

Positive percent agreement: 36.8% (117/318)
 Negative percent agreement: 90.4% (674+14+45+52/868 = 785/868)
 Overall Agreement 76.1% (117+785/1186)

b. *Matrix comparison:*

Both assays use serum as the matrix.

3. Clinical studies:

a. *Clinical Sensitivity and Specificity:*

The study consisted of the following: CD (365), UC (234), and Healthy Normal (587) for a total of 1186 samples.

Differentiation of Crohn's Disease from non-Crohn's Disease (ulcerative colitis and normal controls) Specimens

N=1186		Crohn's Disease	Non-Crohn's Disease	Total
Quanta Lite	Pos	137	63	200
OMP Plus	Neg	228	758	986
ELISA	Total	365	821	1186

Equivocal results counted as negative (i.e. not positive)

Clinical Sensitivity: 37.5% (137/365) (95% CI, 0.325 to 0.427)

Clinical Specificity: 92.3% (758/821) (95% CI, 0.903 to 0.941)

Differentiation of Crohn's Disease from Ulcerative Colitis Specimens

N =599		Crohn's Disease	Ulcerative Colitis	Total
Quanta Lite	Pos	137	26	163
OMP Plus	Neg	228	208	436
ELISA	Total	365	234	599

Equivocal results counted as negative (i.e. not positive)

Clinical Sensitivity: 37.5% (137/365) (95% CI, 0.325 to 0.427)

Clinical Specificity: 88.9% (208/234) (95% CI, 0.841 to 0.926)

The OMP Plus assay is intended as a supplemental assay to ASCA IgG and ASCA IgA. The clinical sensitivities of the new device and the predicate device were tested with both the Quanta Lite™ OMP Plus ELISA and both the Quanta Lite™ ASCA IgG and ASCA IgA ELISA kits.

The simultaneous presence of ASCA IgG, ASCA IgA, and OMP Plus antibodies (triple positive) may prove to be of value for clinical assessment. As shown in the table below, when the whole 510(k) cohort was examined, the presence of at least one of the three markers (ASCA IgG, ASCA IgA, or OMP Plus) resulted in a specificity of 79.4% (652/821), the presence of at least 2 markers resulted in a specificity of 96.3% (791/821), and the presence of all three markers had a

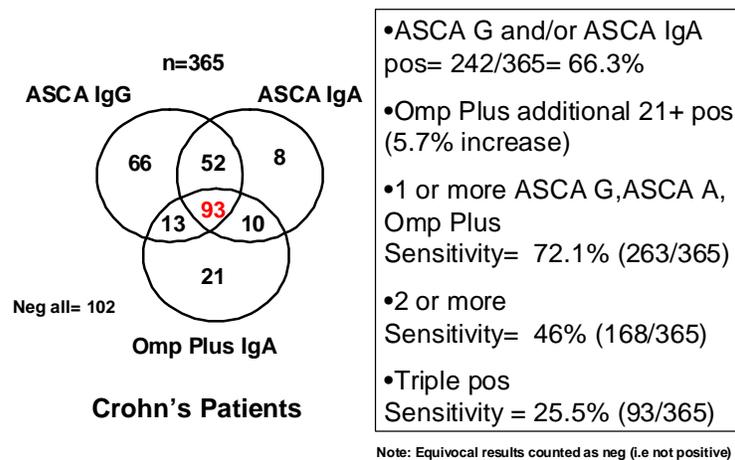
specificity of 99.5% (817/821). The increasing specificity of the marker combination assessment results in decreasing sensitivity. It may however, aid in ruling-in or ruling-out some specimens. For example of the total of 97 triple positive specimens, 93/97 (95.9%) were CD patients. The other 4 consisted of 3 UC and 1 “normal” healthy donor.

At least 1 marker Positive		At least 2 markers positive		3 markers positive	
Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
72.1%	79.2%	46%	96.3%	25.5%	99.5%
(263/365)	(652/821)	(168/365)	(791/365)	(93/365)	(817/821)

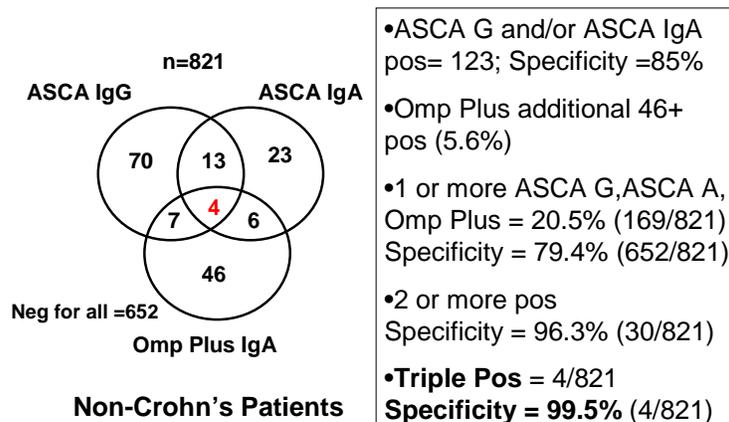
A comparison between the OMP Plus, ASCA IgG, and ASCA IgA demonstrated the added value of the OMP assay results to the results obtained from CD and the ASCA IgG and ASCA IgA is shown in the venn diagrams below.

Fig. 1: Sensitivity of ASCA IgG, ASCA IgA, and OMP for CD, non-CD (and healthy normal), and UC patients.

Crohn's Patients – Whole Cohort

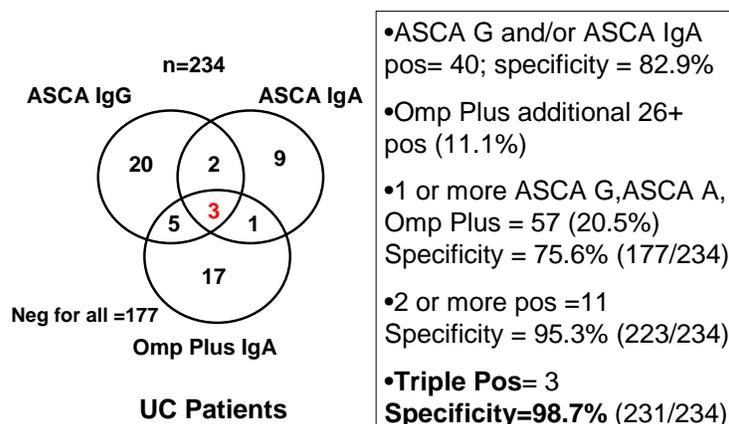


Non-Crohn's Patients



Note: Equivocal results counted as neg (i.e not positive)

Ulcerative Colitis Patients (510K)



Note: Equivocal results counted as neg (i.e not positive)

4. Clinical cut-off:
See assay cut-off
5. Expected values/Reference range:
The expected value in the normal population is negative, however the performance of the assay has not been assessed in patients with Irritable Bowel Syndrome (IBS). The median value obtained from the 500 healthy normal individuals (see assay cut-off) was 12.5 units.

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.