

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

A. 510(k) Number:

k050662

B. Purpose for Submission:

New device

C. Measurand:

Anti-nuclear body protein sp100

D. Type of Test:

Semi-quantitative enzyme-linked immunosorbent assay (ELISA)

E. Applicant:

INOVA Diagnostics

F. Proprietary and Established Names:

QUANTA Lite™ sp100 ELISA

G. Regulatory Information:

1. Regulation section:

21 CFR §866.5090 Antimitochondrial antibody immunological test system

2. Classification:

Class II

3. Product code:

NUM Autoantibodies, nuclear body protein, sp100

4. Panel:

Immunology 82

H. Intended Use:

1. Intended use(s):

The QUANTA Lite™ sp100 kit is an enzyme-linked immunosorbent assay (ELISA) for the semi-quantitative detection of anti-sp100 antibody of the IgG class in human serum. The test is intended to aid in the diagnosis of primary biliary cirrhosis (PBC).

2. Indication(s) for use:

Same as intended use.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Microwell plate reader capable of measuring OD at 450nm and at 620 for dual wavelength readings

I. Device Description:

The QUANTA Lite sp100 ELISA consists of a polystyrene microwell ELISA plate coated with purified sp100 peptide antigen, ELISA negative, low positive and high positive 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™ gp210 ELISA

2. Predicate 510(k) number(s):
k040885
3. Comparison with predicate:

| Similarities | | |
|---------------------|--|--|
| Item | Device | Predicate |
| | Sp100 ELISA | Gp210 ELISA |
| Intended Use | An aid in the diagnosis of primary biliary cirrhosis | Same |
| Method | ELISA | Same |
| Solid phase | Coated polystyrene microwell plates | Same |
| Sample diluent | Tris-buffered saline, Tween 20, absorbents and protein stabilizers | Same |
| Wash concentrate | Tris-buffered saline and Tween 20 | Same |
| HRP IgG conjugate | Goat anti-human IgG | Same |
| Controls | Negative, low positive and high positive | Same |
| Differences | | |
| Item | Device | Predicate |
| | Sp100 ELISA | Gp210 ELISA |
| Analyte detected | Anti-sp100 antibodies | Anti-gp210 antibodies |
| Capture antigen | Purified peptide corresponding to a portion of the sp100 protein | Purified peptide corresponding to a portion of the gp210 protein |

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

None referenced

L. Test Principle:

The assay utilizes plastic microwells as a solid phase for attachment of a purified peptide corresponding to a portion of the sp100 protein to coat the microwells. Pre-diluted controls and diluted patient sera are added to separate wells, allowing any sp100 antibodies present to bind to the immobilized antigen. Unbound sample is washed away and an enzyme labeled goat anti-human IgG antibody is added to each well. A second incubation allows the enzyme labeled anti-human IgG to bind to any patient antibodies which have become attached to the microwells. After washing away any unbound enzyme labeled anti-human IgG, 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 by spectrophotometrically measuring and comparing the color intensity that develops in the patient wells with the color in the control wells. Results determined with the assay are interpreted as negative, equivocal, or positive and are reported in arbitrary units.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
 - a. *Precision/Reproducibility:*

Intra-assay performance for the sp100 ELISA was evaluated by testing 9 specimens a total of 6 times each. The samples tested ranged from 21.0 to 188.3 Units with %CVs ranging from 0.4 to 13.0%.

| | A | B | C | D | E | F | G | H | I |
|------------|-------|------|-------|------|-------|------|------|------|------|
| Mean units | 140.2 | 3.7 | 164.2 | 4.3 | 188.3 | 21.5 | 27.2 | 24.8 | 21.0 |
| SD | 0.58 | 0.46 | 2.48 | 0.56 | 0.88 | 0.54 | 0.57 | 1.40 | 0.73 |
| CV% | 0.4 | 12.2 | 1.5 | 13.0 | 0.5 | 2.5 | 2.1 | 5.6 | 3.5 |

Inter-assay variation was assessed by testing, in duplicate, a panel of 5 specimens twice daily (once in the morning and once in the afternoon) for 3 days. Percent CVs ranged from 3.3 to 4.8 Units.

| | HPC | Spec. 1 | Spec. 2 | Spec. 3 | Spec. 4 | Spec. 5 |
|------------|-------|---------|---------|---------|---------|---------|
| Mean units | 139.5 | 141.4 | 4.3 | 172.2 | 4.7 | 197.9 |
| SD | 6.1 | 6.7 | 0.1 | 8.1 | 0.2 | 8.5 |
| CV% | 4.4 | 4.8 | 3.3 | 4.7 | 3.7 | 4.3 |

b. Linearity/assay reportable range:

No claims were made regarding linearity for the assay. It is a semi-quantitative assay with results reported out as negative (0.0 – 20.0 Units), positive (≥ 25 Units), or equivocal: (20.1 – 24.9 Units) when results are interpreted by comparison to the low positive control value of 25 Units. Specimens giving OD readings above the readable range of the plate reader may be reported as greater than the highest measurable OD. Alternatively, the sample may be diluted, re-run and a calculated value obtained.

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

There is no recognized standard or reference material for anti-sp100 antibodies.

d. Detection limit:

The determination of detection limit/analytical sensitivity is not relevant and was not performed for this assay.

e. Analytical specificity:

Interference studies were not performed. The package insert stated microbially contaminated, heat-treated, samples with visible particulate, grossly hemolyzed or lipemic specimens should not be used in the assay.

Cross-reactivity study to other autoantibodies was performed. Results were under in section for “Clinical Specificity”.

f. Assay cut-off:

Serum samples from a panel of 272 asymptomatic, healthy individuals were tested. The panel included subjects from the US. Age and sex data were available for 192 of the specimens, and unavailable for 80 specimens. The ages ranged from 18-78 years and included 87 females and 105 males. The average value for the normal population was 5.8 units and the median value was 4.8 units. Using a cut-off for negative of ≤ 20 units, with the exception of

2 specimens, all specimens were negative. Of the 2 specimens interpreted as positive, one was a low positive of 28.5 units and one was a very strong positive with a value of 134 units. Indirect immunofluorescent examination of the 2 specimens on HEp-2 cells showed that the strongly reactive sample had a classic nuclear dot pattern typical of sp100 antibodies. The weak positive sample had an unclear pattern.

2. Comparison studies:

a. *Method comparison with predicate device:*

The sponsor submitted comparison data for 359 subjects that included 201 PBC patients (PBC, PBC/AIH, and AIH/PBC overlap), 4 patients suspected of having PBC, 99 normal subjects, and 55 non-PBC disease control subjects.

| N=359 | QUANTA Lite gp210 ELISA | | | |
|--------------------------------|--------------------------------|-----------|-----|-------|
| Quanta Lite sp100 ELISA | + | Equivocal | - | Total |
| + | 13 | 2 | 43 | 58 |
| Equivocal | 0 | 0 | 7 | 7 |
| - | 34 | 6 | 254 | 294 |
| Total | 47 | 8 | 304 | 359 |

The positive percent agreement was 27.6% (13/47) and the negative percent agreement was 85.5% (43/287). The overall agreement was 77.6% (267/344). Equivocals were excluded from the calculations. Both assays were 100% negative for all non-PBC samples. The overall agreement between the assays was low because the assays measure different analytes and not all PBC patients have both antibodies. Sp100 and gp210 antibodies can both be present in some PBC patients, but can be independent markers of PBC.

b. *Matrix comparison:*

Both assays use only serum as matrix.

3. Clinical studies:

a. *Clinical Sensitivity:*

Clinical sensitivity was established by testing sera from 273 PBC or PBC/AIH subjects. The overall clinical sensitivity of the assay was 24.5% (67/273 with 7 equivocal results considered as negative).

| Clinical Status | N = | Sp100 ELISA positive | Sp100 ELISA equivocal | Sp100 ELISA negative |
|-----------------------------|-----|----------------------------|-----------------------------|----------------------------|
| PBC | 266 | 65 | 7 | 194 |
| PBC/AIH | 2 | 0 | 0 | 2 |
| PBC?, PBC/AIH?, AIH?/PBC | 5 | 2 | 0 | 3 |

b. *Clinical specificity:*

A total of 383 sera from patients with non-PBC liver disease, autoimmune, other conditions (n=111) and normal subjects (n=272) were tested to assess potential cross-reactivity of other disease sera with the assay.

| Non-PBC or PBC/AIH | N = | Sp100 positive | Sp100 equivocal | Sp100 negative |
|---------------------------|------------|-----------------------|------------------------|-----------------------|
| HBV, HCV | 6 | 0 | 0 | 6 |
| SLE | 36 | 0 | 2 | 34 |
| AIH 1, AIH/PSC?, AIH 2 | 43 | 0 | 0 | 43 |
| RA | 3 | 0 | 0 | 3 |
| PSC, PSC? | 3 | 0 | 0 | 3 |
| Misc. autoantibodies:* | 16 | 0 | 0 | 16 |
| Diagnosis uncertain | 4 | 0 | 0 | 4 |
| Normal | 272 | 2 | 0 | 270 |
| Total | 383 | 2 | 2 | 379 |

* Sm (1), RNP (1), SSB (1), Histone (3), Scl-70 (1), ribosome P (1), chromatin (2), centromere (1), ASCA (2), GBM (2), Jo-1 (1)

The clinical sensitivity of the new device (24.5%) was supported by the published literature. The literature also supports the fact that an anti-sp100 antibody assay may detect a subpopulation of PBC patients that are negative for anti-mitochondrial antibodies (AMA) by IFA and/or negative for Mitochondrial-2 (M2) antibodies measured by ELISA.

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

Not applicable.

4. Clinical cut-off:

See assay cut-off and expected values.

5. Expected values/Reference range:

The expected result in the normal population is negative (≥ 20 Units). The prevalence of PBC ranges from estimates of 2 per 100,000 in Japan and Australia to 40 per 100,000 in the US.

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.