

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

**A. 510(k) Number:**

k052793

**B. Purpose for Submission:**

Modification to a Cleared Device

The device modification was for changing the ImmunoCAP™/UniCAP Specific IgA Conjugate from polyclonal rabbit anti-human IgA antibodies to mouse monoclonal anti-human IgA antibodies. There were no changes to the specific IgG conjugate. The name of the device was changed from UniCAP to ImmunoCAP/UniCAP.

**C. Measurand:**

Human anti-IgA and anti-IgG Gliadin Antibodies.

**D. Type of Test:**

Semi-quantitative, Non Competitive Solid Phase, Fluoroenzymeimmunoassay (FEIA)

**E. Applicant:**

Pharmacia Diagnostics AB

**F. Proprietary and Established Names:**

ImmunoCAP™/UniCAP Gliadin IgA/IgG

ImmunoCAP™/UniCAP Specific IgA

**G. Regulatory Information:**

1. Regulation section:

21 CFR 866.5750- Radioallergosorbent Immunological Test System

2. Classification:

Class II

3. Product code:

MST- Antibodies, Gliadin

4. Panel:

Immunology 82

**H. Intended Use:**

1. Intended use(s):

ImmunoCAP/UniCAP Gliadin IgA/IgG is a device for the in vitro semiquantitative measurement of IgA and IgG antibodies specific for Gliadin in human serum. ImmunoCAP/UniCAP Gliadin IgA/IgG is intended to be used with the instrument ImmunoCAP/UniCAP together with reagents as stated in the Directions for Use provided with ImmunoCAP/UniCAP Specific IgA and ImmunoCAP/UniCAP Specific IgG. It is intended for in vitro diagnostic use as an aid in the clinical diagnosis of patients with celiac disease.

ImmunoCAP™/UniCAP Specific IgA is an in vitro test system for quantitative measurement of antigen specific IgA antibodies. The corresponding antigen for the specific antibody to be measured by ImmunoCAP/UniCAP Specific IgA is bound to the Antigen ImmunoCAP solid phase component of the ImmunoCAP/UniCAP Specific IgA System. ImmunoCAP/UniCAP Specific IgA assay is to be used with the instrument ImmunoCAP100/UniCAP 100. It is intended for in vitro diagnostic use in conjunction with other clinical findings, and

is to be used in clinical laboratories as well as physician's office laboratories.

2. Indication(s) for use:  
Same as Intended use.
3. Special conditions for use statement(s):  
The device is for prescription use only.
4. Special instrument requirements:  
ImmunoCAP100/UniCAP100

**I. Device Description:**

The device consists of specific IgA and IgG conjugate, specific IgA/IgG sample diluent, specific IgA/IgG calibrators, two specific IgA curve controls, individual antigens covalently coupled to solid phase (Antigen ImmunoCAP Gliadin), development kit including development solution and stop solution and system washing solution.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):  
UniCAP Gliadin IgA (UniCAP Specific IgA)
2. Predicate 510(k) number(s):  
k982533
3. Comparison with predicate:

<b>Similarities</b>		
Item	New Device	Predicate
Device Name	ImmunoCAP	UniCAP
Intended Use Statement	In vitro semiquantitative measurement of IgA and IgG antibodies specific for Gliadin in human serum used with the instrument ImmunoCAP/UniCAP. It is intended for in vitro diagnostic use as an aid in the clinical diagnosis of patients with celiac disease.	Same
Results	Semi- quantitative interpretation	Same
Instrumentation	Same (Except for new brand name ImmunoCAP™)	UniCAP 100
Sample Type	Human Serum	Same
Measuring Principle	Non Competitive Solid Phase (FEIA)	Same
Measuring Range	1-100 mg/l	Same
Number of Immunological Reactions Steps	2	Same
Reaction Temperature	37 °C	Same

Similarities		
Item	New Device	Predicate
Sample Dilution	1:100	Same
Capture Antigen	Wheat Extract	Same
Calibrators	Human IgA Calibrators	Same
Calibration Curve	Option to store curve for up to one month	Same
Stability		
Reference Standards	International Ref. Prep. 67/86 for Human Serum Immunoglobulin A,G and M from WHO	Same
Controls	Two IgA curve controls included in kit	Same

Differences		
Item	New Device	Predicate
Detection Antibody (Specific IgA Conjugate)	Mouse Monoclonal anti-Human IgA antibodies	Rabbit Polyclonal anti-Human IgA antibodies

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

None referenced.

**L. Test Principle:**

The gliadin antigen is covalently coupled to ImmunoCAP and reacts with specific antibodies in the patients diluted serum sample. After washing away non specific antibodies, enzyme-labeled antibodies against IgA are added to form a complex. After incubation, unbound enzyme-anti-IgA is washed away and the bound complex is incubated with a developing agent. After stopping the reaction, the fluorescence of the eluate is measured. The response value is proportional to the amount of specific IgA present in the specimen. To evaluate the test results, the response for the patient samples are transformed to concentrations with the use of a calibration curve.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

a. *Precision/Reproducibility:*

Three samples with various concentration levels were assayed in 4 replicates with 3 lots of conjugate at 6 different times. The percents coefficient variations (%CV) within assay and between assays are summarized below:

Sample Level (mg/L)	% CV Within Assay	% CV Between Assays
3	6.8	7.7
18	3.3	3.2
32	4.5	4.4

b. *Linearity/assay reportable range:*

The assay reportable range is 1-100 mg/L

#### Dilution Studies

The goal of the study was to test if sample concentrations are correctly measured after dilution in UniCAP Specific IgA when using UniCAP Specific IgA Conjugate containing monoclonal antibodies. Three samples were diluted 1/100 and then further diluted 1:2, 1:4, 1:8 and 1:16. Fifteen samples were diluted 1/100 and then further diluted 1:5.5. IgA/IgG diluent was used for the dilution. All dilutions were tested in 3 runs, in 3 replicates/run in UniCAP 100. Calibrators were run in 2 replicates/run. The O/E (obtained sample concentration/expected sample concentration) results were within the specification ( $\leq 20\%$ ). For dilutions 1:2 and 1:4 all three samples were within specifications. Seventy-four percent (74%) of the different dilutions, including the 1:5.5 dilutions, were within specifications (20%). Values outside target value were obtained in the low concentration range. Since it is necessary to dilute samples with high titers only, the results are considered to be acceptable.

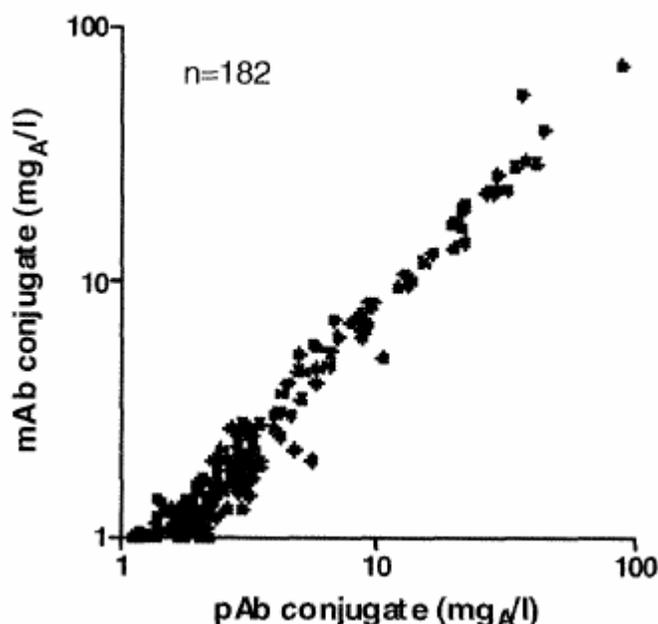
- c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*  
The calibrators are traceable to the International Reference Preparation 67/86 for Human Serum Immunoglobulin A, G, and M from WHO.
- d. *Detection limit:*  
Three verification lots of UniCAP Specific IgA Conjugate and new monoclonal mouse anti-human IgA conjugate were tested. Each verification lot was tested with new conjugate in the same run. Calibrator 0.01 mg/L and ImmunoCAP IgA/IgG calibrators were tested in 12 replicates with each conjugate. The detection limit was determined using the discriminatory ability (D). D was determined according to the formula:

$$\frac{\text{Calibrator } 0.01 - \text{Diluent}}{\sqrt{S^2_{\text{Calibrator } 0.01} + S^2_{\text{Diluent}}}} = D$$

If D is  $\geq 2$ , the test is capable of discriminating IgA/IgG sample diluent from the calibrator (0.01 mg/L). Based on the test results the discrimination was significant between sample diluent and calibrator 0.01 mg/L for all three lots. The detection limit for UniCAP Specific IgA is 0.01 mg/L.

- e. *Analytical specificity:*  
Cross-reactivity: There was no detectable cross-reactivity with human serum immunoglobulins IgG, IgM or IgE at normal physiological levels.
  - f. *Assay cut-off:*  
In a study with 100 healthy individuals, 90% had results  $< 1.6$  mg/L and 95% had results  $< 2.2$  mg/L.
2. Comparison studies:
- a. *Method comparison with predicate device:*  
One hundred eighty-two samples (90 celiac disease patients, 48 non celiac disease and 44 non atopic healthy blood donors) were tested with the mouse monoclonal antibody (mAb) and the polyclonal antibody (pAb) conjugates.

The anti-Gliadin antibody concentrations ranged from 1-100 mg/L. Sample concentrations of the two conjugates were compared and the linear regression analysis yielded results (mAb) = 0.85(pAb) - 0.37 and R<sup>2</sup>=0.95 (see figure below)



Since on average, the Gliadin specific IgA antibody results using the mAb conjugate were 30 % lower than the present pAb conjugate the assay cut-off has to be adjusted to 2 mg/L to be comparable to the predicate device. The comparison table below shows the results for samples tested with mAb specific IgA conjugate and the pAb conjugate in the predicate device using a cut-off of 3 mg/L for the predicate device and 2 mg/L for the modified assay. The 2 mg/L is the specified cut-off for anti-Gliadin IgA in the ImmunoCAP<sup>TM</sup>/UniCAP Gliadin IgA/IgG and ImmunoCAP<sup>TM</sup>/UniCAP Specific IgA Package Inserts. The total agreement between the new mAb conjugate and the pAb was 91.2 %.

		pAb IgA Conjugate		
		≥3	<3	Total
mAb IgA Conjugate	≥2	71	9	80
	<2	7	95	102
	Total	78	104	182

Overall percent agreement is  $(166/182) \times 100 = 91.2\%$   
 Positive percent agreement is  $(71/78) \times 100 = 91.0\%$   
 Negative percent agreement is  $(95/104) \times 100 = 91.3\%$

b. Matrix comparison:

Both assays use human serum as matrix.

3. Clinical studies:
  - a. *Clinical Sensitivity:*  
Not provided.
  - b. *Clinical Specificity:*  
Not provided.
  - c. *Other clinical supportive data(when a and b are not applicable):*  
Not applicable.
4. Clinical cut-off:  
See Assay cut-off
5. Expected values/Reference range:  
The Expected value in the normal population would be <2mg/L. At this cut-off, 93% of the subjects tested were 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 substantial equivalence decision.