510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
K062746

B. Purpose for Submission:
New device

C. Measurand:
Ferritin

D. Type of Test:
Particle enhanced immunoturbidimetry

E. Applicant:
Medicon Hellas SA

F. Proprietary and Established Names:
Medicon Ferritin - LATEX

G. Regulatory Information:
1. Regulation section:
   21 CFR 866.5340 Ferritin immunological test system
2. Classification:
   Class II
3. Product code:
   DBF Ferritin, antigen, antiserum, control
4. Panel:
   Immunology (82)

H. Intended Use:
1. Intended use(s):
   The Medicon Ferritin – LATEX is an i*n vitro* diagnostic reagent intended for the determination of Ferritin in human serum and plasma using Olympus AU400/600/640 automated clinical chemistry analyzers.
2. Indication(s) for use:
   Medicon Ferritin – LATEX reagent is for the determination of ferritin in human serum and plasma using automated clinical chemistry analyzers. The measurement of ferritin may aid in the diagnosis of diseases affecting iron metabolism.
3. Special conditions for use statement(s):
   Prescription use
4. Special instrument requirements:
   Olympus Clinical Chemistry Analyzers, Models AU400/600/640

I. Device Description:
The Ferritin – LATEX reagents consist of R1: 120 nM Tris buffer pH=8.2, accelerator, surfactant, stabilizers and preservatives; and R2: latex particles coated with rabbit anti-human ferritin in 20 nM Tris buffer pH=8.4, stabilizers and preservatives.

J. Substantial Equivalence Information:
1. Predicate device name(s):
   Olympus Ferritin Reagent
2. Predicate 510(k) number(s):
   k030124
3. Comparison with predicate:

Similarities		
Item	**New Device** Medicon Ferritin	**Predicate** Olympus Ferritin k030124
Indication for use	Medicon Ferritin – LATEX reagent is for the determination of ferritin in human serum and plasma using automated clinical chemistry analyzers. The measurement of ferritin may aid in the diagnosis of diseases affecting iron metabolism.	Reagent for the determination of ferritin concentrations in human serum using the Olympus family of clinical chemistry analyzers. Serum ferritin is an indicator of body iron stores: Measurements of ferritin aid in the diagnosis of diseases affecting iron metabolism, such as hemochromatosis (iron overload) and iron deficiency anemia.
Constituents	Ferritin R1 (Buffer) Ready to Use Ferritin R2 (Latex) Ready to Use	Same
Storage conditions	Refrigerate at 2 º - 8º C until expired	Same
Methodology	Particle enhanced immunoturbidimetry	Same
Instrument family	Olympus Clinical Chemistry Analyzers	Same
Formulation	Final reactive ingredients: Tris Buffer pH: 8.2 Latex particles coated with rabbit anti-human ferritin Preservative	Same

Similarities		
Item	**New Device** Medicon Ferritin	**Predicate** Olympus Ferritin k030124
Calibrator – recommended but not included with kit	Olympus Serum Protein Multi-Calibrator ODR3021	Same
Controls – recommended but not included with kit	Olympus ITA Control Sera, ODC0014, ODC0015, ODC0016	Same
Reagent Stability	On board: 30 days	Same
Calibration Interval	After each lot and 14 days	Same
Reference Intervals	Serum / Plasma: Infants – 1 month: 6-400 ng/mL 1 month – 6 months: 6-410 ng/mL 6 months – 12 months: 6–80 ng/mL 1 year – 5 years: 6–60 ng/mL 6 years – 19 years: 6–320 ng/mL adult men: 20-250 ng/mL adult women:20-200 ng/mL	Same (for serum only)
Traceability/ Standardization	Standardized against the WHO 3rd International Standard for ferritin, Recombinant NBSC code: 94/572.	Same

Differences		
Item	**New Device** Medicon Ferritin	**Predicate** Olympus Ferritin K030124
Measuring Range	4 – 450 ng/ml	8 – 450 ng/ml
Sample type	Serum and plasma	Serum

K. Standard/Guidance Document Referenced (if applicable):
None referenced

L. Test Principle:
When a sample containing ferritin is mixed with the Ferritin - LATEX reagent and the reaction buffer included in the kit, ferritin reacts with the antibodies leading to agglutination of the latex particles. The agglutination is detected as turbidity change (the decrease of transmitted light caused by the aggregates measured at 600 nm) and is directly proportional to the concentration of ferritin in the sample.

M. Performance Characteristics (if/when applicable):
1. Analytical performance:
   a. *Precision/Reproducibility:*
      A precision study was performed on an OLYMPUS AU640 Clinical Chemistry Analyzer using OLYMPUS ITA Control Levels (Low, Medium, and High). The within run, between run, and total %CV were calculated according to CLSI (NCCLS) EP5-A protocol.

	Within Run			**Total**		
	Level 1	Level 2	Level 3	Level 1	Level 2	Level 3
Mean (ng/mL)	38.0	108.1	224.1	38.0	108.1	224.1
SD	1.22	1.42	2.23	1.50	1.75	3.20
% CV	3.20	1.31	0.99	3.94	1.62	1.43

   b. Linearity/assay reportable range:
      Linearity was performed on an OLYMPUS AU640 Clinical Chemistry Analyzer according to CLSI (NCCLS) EP6-P Guideline. A serum sample with high Ferritin level was serially diluted and each of the 14 dilutions was assayed in quadruplicate on the Olympus AU 640. The acceptance criterion is ± 10% deviation from regression line. The percent deviation from the regression line for the 14 points ranged from -10.2 to 3.1%. The assay is linear over the reportable range of 4-450 ng/ml.

Prozone Effect: High pool of Ferritin (SCIPAC) was diluted with saline. No hook effect was observed for the tested specimen at 10,000 ng/ml compared to the upper limit of the measuring range of 450 ng/mL.

c. Traceability, Stability, Expected values (controls, calibrators, or methods): The recommended calibrator is standardized against the WHO 3rd International Standard for ferritin, Recombinant NBSC code: 94/572.

d. Detection Limit:
The <u>Lowest Detectable Level</u> was defined as the Mean (20 replicates) + 3SD = $0.8 + 3(0.9) = 3.4$ ng/mL. Detection Limit is stated at 4.0ng/mL.
<u>Functional Lower Limit</u> is estimated to be 4.0ng/mL. A serum with initial concentration value of 58.7ng/mL was serially diluted 1:1 with saline (0.9g NaCl /100ml).

e. Analytical specificity:
<u>Interference</u>: Interference testing was performed by spiking levels of each interferant into pooled serum. Acceptance criterion was set at $\leq \pm 10\%$ (Final/Original results x 100%).
- Ascorbic Acid: Less than 5% up to 3 mg/dL ascorbic acid
- Hemolysis: Less than 5% up to 500 mg/dL hemoglobin.
- Lipemia: Less than 10% up to 400 mg/dL Intralipid®.
- Icterus: Less than 5% up to 20 mg/dL bilirubin.
- Rheumatoid Factor: Less than 5% up to 900 IU/ml RF.

f. Assay cut-off:
Not applicable

2. <u>Comparison studies:</u>
a. *Method comparison with predicate device:*
One hundred seventy-six (176) patient serum samples ranging from 7.50 - 491.40 ng/mL were analyzed using Ferritin-LATEX and Olympus Ferritin Reagent (predicate device) on an OLYMPUS AU 640 Clinical Chemistry Analyzer. No artificially prepared samples were used in this study. The following results were obtained using Linear Regression Analysis: $y = 1.0016x + 4.3849$ ng/mL with a correlation coefficient of R= 0.9958.

b. *Matrix comparison:*
40 patient plasma (EDTA) ferritin samples ranging from 8.90 - 482.85 ng/mL were compared to serum ferritin values obtained using Medicon Ferritin-LATEX on an OLYMPUS AU 640 Clinical Chemistry Analyzer. The following results were obtained using Linear Regression Analysis: $y = 0.9847x - 1.1275$ ng/mL, with a correlation coefficient of R= 0.9978.

138 patient plasma (LiH) ferritin samples ranging from 5.6 - 477.50 ng/mL were compared to serum ferritin values obtained using Medicon Ferritin-

LATEX on an OLYMPUS AU 640 Clinical Chemistry Analyzer. The following results were obtained using Linear Regression Analysis:
$y = 0.9778x + 1.2886$ ng/mL, with a correlation coefficient of R= 0.9988.

3. Clinical studies:
    a. *Clinical Sensitivity:*
       Not determined
    b. *Clinical specificity:*
       Not determined
    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:
   Reference ranges were taken from Tietz:
   1. Tietz, NW, ed. Clinical Guide to Laboratory Tests. 3rd. ed Philadelphia: W.B. Saunders Company Ltd., 1995.
   2. Burtis, CA and Ashwood, ER, ed. Tietz Textbook of Clinical Chemistry. 2nd. ed. Philadelphia: W.B. Saunders Company Ltd., 1994.

   Serum / Plasma:
   Infants – 1 month: 6-400 ng/mL
   1 month – 6 months: 6-410 ng/mL
   6 months – 12 months: 6–80 ng/mL
   1 year – 5 years: 6–60 ng/mL
   6 years – 19 years: 6–320 ng/mL
   Adult men: 20-250 ng/mL
   Adult women: 20-200 ng/mL
   As stated in the product insert, each laboratory should determine its own expected values as dictated by GLP.

N. Proposed Labeling:
The labeling is sufficient and 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.