510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k050596

B. Purpose for Submission:
This is a new device.

C. Measurand:
Alpha-1 Antitrypsin

D. Type of Test:
Quantitative latex enhanced turbidimetric assay

E. Applicant:
Biokit S.A.

F. Proprietary and Established Names:
Quantia A1-AT
Quantia Proteins Control
Quantia Proteins Standard

G. Regulatory Information:

1. Regulation section:
   21CFR§ 866.5130, Alpha-1-antitrypsin Immunological Test System.
   21CFR§ 862.1660, Quality Control Material (Assayed and Unassayed)
   21CFR§ 862.1150, Calibrator
2. Classification:
   Device and calibrator - Class II
   Quality control material - Class I
1. Product code:
   DEM, Alpha-1-antitrypsin, Antigen, Antiserum, Control
   JJX, Single (Specified) Analyte Controls (Assayed and Unassayed)
   JJS, Calibrator, Primary
4. Panel:
   Immunology (82)
   Chemistry (75)

H. Intended Use:

1. Intended use(s):
   The Quantia A1-AT is intended for the in vitro quantitative determination of alpha-1 antitrypsin concentration in human serum or plasma (heparin with or without gel separator, EDTA) on the AEROSET® system as an aid in the diagnosis of juvenile and adult cirrhosis of the liver and pulmonary emphysema.

   Quantia Proteins Control is intended for use in monitoring the quality control of results obtained with the Quantia A1-AT reagents by turbidimetry. For *in vitro* diagnostic use.

   Quantia Proteins Standard is intended for use in establishing calibration

curve for the Quantia A1-AT reagents by turbidimetry. For *in vitro* diagnostic use.

2. Indication(s) for use:
   Same as above
3. Special conditions for use statement(s):
   For prescription use only.
4. Special instrument requirements:
   For use in the Aeroset® system (k980367).

I. Device Description:

Quantia A1-AT consists of the following:

- A1-AT R1 buffer whose reactive ingredients are Tris buffer, polyethylene glycol detergent, and sodium azide.
- A1-AT R2 reagents whose reactive ingredients are anti-human A1-AT goat serum, Tris buffer, detergent, and sodium azide.

The Quantia Proteins lyophilized controls I and II are prepared from human sera containing human A1-AT, human Beta-2-Microglobulin and gentamicin sulphate.
The Quantia Proteins standards are ready to use calibrators prepared with human A1-AT at 5 different levels in a Hepes-glycine buffer. The concentrations in mg/dL and g/L are indicated on the standard data sheet.

The controls and standards are sold separately.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   N Antisera to Human alpha -1-antitrypsin and a_2 Macroglobulin (Dade Behring)
2. Predicate 510(k) number(s):
   k860894
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
	Quantia A1-AT	**N Antisera to Human alpha -1-antitrypsin and a_2 Macroglobulin (Dade Behring)**
Intended Use	Quantitative in vitro diagnostic determination of alpha1-antitrypsin	Same
Storage conditions	Refrigerate at 2-8^{o}C until expired	Same
Standardization	International Material for	Same

Similarities		
Item	Device	Predicate
	Measurement of 14 Human Serum Proteins (CRM 470).	
Components	Controls and standards are sold separately.	Same

Differences		
Item	Device	Predicate
Sample type	Serum and plasma (EDTA, heparin with and without gel separator)	Serum only
Methodology	Latex enhanced turbidimetry	Nephelometry
Controls	Lyophilized human sera with A1-AT at 2 levels	Liquid stabilized human sera at 3 levels
Calibrators	Hepes-glycine buffer containing A1-AT at 5 different levels.	3 levels of stabilized human sera

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

None referenced.

L. Test Principle:

The Quantia A1-AT reagent is a goat serum anti-human alpha 1 – antitrypsin which reacts specifically with the alpha 1 – antitrypsin of the sample to yield an insoluble aggregate which can be measured by turbidimetry. Results are expressed in mg/dL or g/L based on the International Reference Material CRM 470.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The precision study was performed on an AEROSET® System using the Quantia Proteins Control (low and High) and a mixture of both, run in duplicate twice a day over 20 days (n=80). This experiment was performed by one operator on one site with one lot of reagent.

N	Mean (mg/dL)	Within run %CV	Between-run %CV	Total %CV
80	77.7	1.2	0.2	1.4
80	156.9	0.7	0.1	0.8
80	229.7	1.3	0.6	1.8

b. Linearity/assay reportable range:

Linearity testing was performed on an AEROSET® System using a serum sample containing 280 mg/dL of A1-AT diluted in physiologic saline at 10 different dilutions. Each dilution was analyzed in quintuplicate. Testing was done with the automatic and without automatic rerun capability. The reported means were calculated from the pooled results. Data showed a regression equation $Y = 1.001X – 0.3$, r^2 of 0.9995 for the "without the automatic rerun capability." Linearity was set at 25 to 300 mg/dL

The AEROSET® System can automatically rerun samples with results above the upper limit of the valid range (300 mg/dL) at 1:5 sample dilutions. . The instrument then automatically recalculates the new sample result. To assess the extended linearity range, a serum spiked with partially purified Alpha-1 Antitrypsin (Sigma) was prepared. Ten dilutions in physiologic saline were done and analyzed in quintuplicate. The regression equation for the automatic rerun capability showed $Y = 0.994X + 5$, $r^2 = 0.9984$. Linearity was set at 25 to 1261 mg/dL.

The graphs showed the curves are linear on both settings.

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

The reference material is the BCR Reference Material Proteins, CRM 470. The calibrator is supplied by Strategic BioSolutions. Values are assigned based on CRM 470 CAP/IFCC Lot 91/0619. The concentration of A1-AT of each new lot of product is tested and reviewed by the Quality Control Department of Biokit, using the Quantia A1-AT reagents. Once this lyophilized material is reconstituted, it is aliquoted and stored frozen at -20°C. Two lots of Quantia A1-AT are used to test the concentration of each new lot of calibrators. The concentration value of each new lot of Quantia Proteins Standard obtained has to be within ±10% of the initial value stated by Strategic solutions.

The controls are bulk manufactured by BioRad which has been cleared (k851202/A1) under the trade name Lypochek Immunology Plus Control. Target values and acceptance ranges are assigned to each level of Quantia Proteins Control by the Quality Control Department of Biokit. Two different lots of Reagent and one lot of calibrator are used. Upon calibration, each level of the new lot of Quantia Proteins Control to be assigned is tested 10 times with each lot of reagent. The acceptance value is the target value ± 20% for both controls (low and high levels).

Stability studies were performed and the following conclusions were obtained:

- On-Board Instrument Stability – The reagents Quantia A1-AT

Buffer (R1) and Quantia A1-AT Reagent (R2) are stable on – board the instrument for 5 weeks at 15°C.

- Calibration Stability – The data and the graph indicate that the calibration is stable for at least 30 days.
- Reconstituted Control Stability – The data indicate that Quantia Proteins Control I and II is stable for at least 15 days at 2-8°C after reconstitution.
- Reagent Shelf-Life Stability – Shelf life stability of the reagents was conducted up to 18 months with three different lots. Recovery showed minimal change from baseline and the final shelf-life stability was 12 months at 2-8°C.

d. Detection limit:

Detection limit was calculated by running 30 replicates of physiologic saline on an AEROSET® System. The mean and the standard deviation were calculated. The detection limit is defined as the mean reported value for the physiologic saline plus 2 SD. The Detection Limit was found to be 0.38 mg/dL.

Limit of quantification was also performed on an AEROSET® System using 5 dilutions of the 31 mg/dL Quantia Proteins Standard in physiologic saline. Each dilution was run in quintuplicate. The data support the claim for a limit of quantification of 25 mg/dL. A limit of quantification is the smallest concentration of unknown that can be reliably be quantified by the instrumental method.

e. Analytical specificity:

Interference: Interference testing was performed on an AEROSET® System by spiking a sample containing A1-AT. For each interfering substance, the sample was split in two aliquots, one spiked with a concentrated interfering substance and the other with the control buffer. Each aliquot was analyzed 10 times with a single lot of Quantia A1-AT reagent. No significant interference was observed in:

- Hemoglobin up to 460 mg/dL
- Bilirubin up to 19.6 mg/dL
- Triglycerides up to 1327 mg/dL
- Turbidity of sample up to 2.33 AU/cm at 660 nm.
- Rheumatoid Factor interference is below 10% up to 800 IU/mL.

No cross-reactivity studies have been conducted with heterophile antibodies.

f. Assay cut-off:

Not provided.

2. Comparison studies:

a. Method comparison with predicate device:

The table below shows the comparison of serum samples (N=111) that were tested with the Quantia A1-AT and the predicate device Dade Behring N Antisera to Human A1-AT. The samples were obtained from the Biochemistry Department and Emergency Room of the Hospital de

Sant Pau (Barcelona) and also from the Blood Bank of the Hospital de la Vall Hebro` (Barcelona). No information about age and gender was provided. The sample concentrations cover the entire clinical range. The required specifications were: Slope 1.0± 0.20; r = 0.950

	AEROSET® vs. BNII (Dade-Behring)
Slope	1.002 (95% CI: 0.973 to 1.030)
Intercept	12.2 (95% CI: 5.8 to 18.6)
Range (mg/dL)	42.0-442.5
Mean X (mg/dL)	205.7
Mean Y (I mg/dL)	218.2
r	0.9890
S_{YX}	13.7
N	111

b. Matrix comparison:
Four fresh samples were collected from each 25 individuals: no antocoagulant, Li-Heparin, Li-Heparin with Gel Sep and K-EDTA. Each sample was analyzed in duplicate with Quantia A1-AT on the Aeroset® system. The results of the linear regression analyses are seen on the table below.

N=25	**Li-Heparin**		**Li-Heparin Gel Separator**		**EDTA**	
		95% CI		95% CI		95% CI
Intercept	-2.1	-6.9 to 2.8	1.4	-3.0 to 5.7	2.6	-1.8 to 6.9
Slope	0.944	0.913 to 0.976	0.922	0.894 to 0.951	0.951	0.922 to 0.979
Correlation	0.997	0.993 to 0.999	0.997	0.994 to 0.999	0.998	0.994 to 0.999

3. Clinical studies:
   a. Clinical Sensitivity:
   Not applicable
   b. Clinical specificity:
   Not applicable
   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:
   The reported expected range for alpha 1-antitrypsin in adults (90-200 mg/dL) is from a literature:
   Dati F. Schumann G,Thomas L, et al. Consensus of a Group of Professional Societies and Diagnostic Companies on Guidelines for Interim Reference Ranges for 14 Proteins in Serum base on the Standardization against the IFCC/BCR/CAP Reference Material (CRM 470). Eur J Clin Chem Biochem 34:517-520, 1996.

   Each laboratory should establish its own normal ranges since values may differ depending on the population studied.

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.