510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k050493

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

C. Measurand:
Immunoglobulins IgE

D. Type of Test:
Particle-latex enhanced immunoturbidimetric assay, quantitative

E. Applicant:
Biokit S.A.

F. Proprietary and Established Names:
Quantia IgE
Quantia Ferritin/Myoglobin/IgE Control
Quantia IgE Standard

G. Regulatory Information:

1. Regulation section:
   21CFR§ 866.5510 Immunoglobulins A,G,M,D,E, 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:
   DGC, IgE, 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 IgE is intended as a latex particle enhanced immunoturbidimetric assay for the *in vitro* quantitative determination of Immunoglobulin E concentration in human serum or plasma (EDTA,

heparin, citrate) on the AEROSET® system as an aid in the diagnosis of IgE mediated allergic disorders in conjunction with other clinical findings.

Quantia Ferritin/Myoglobin/IgE Control is intended for use in monitoring the quality control of results obtained with the Quantia IgE reagents by turbidimetry. For *in vitro* diagnostic use.

Quantia Proteins Standard is intended for use in establishing calibration curve for the Quantia IgE 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 IgE consists of IgE R1 buffer and IgE R2 reagents (latex particle coated with mouse anti-human IgE, and sodium azide).

The Quantia Ferritin/Myoglobin/IgE lyophilized controls I and II are prepared from human sera containing human ferritin, myoglobin and IgE, and sodium azide. [These controls were FDA cleared for use with Quantex Ferritin (k040879) and for Quantex Myoglobin (k042982)].

The Quantia IgE standards are ready to use calibrators prepared with human IgE at 5 different levels in a Hepes-glycine buffer. The concentrations in IU/mL are indicated on the standard data sheet.

The controls and standards are sold separately.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Pharmacia Total IgE Reagent on Unicap 100
2. Predicate 510(k) number(s):
   k964152
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
	Quantia IgE	**Pharmacia Total IgE Reagent on Unicap 100**
Intended Use	Quantitative determination of IgE	Same
Storage conditions	Refrigerate at 2-8^{o}C until	Same

Similarities		
Item	Device	Predicate
	expired	
Standardization	2nd WHO International Reference Preparation IgE code 75/502(CRM 470).	Same
Components	Controls and standards are sold separately.	Same
Sample type	Serum and plasma	Same

Differences		
Item	Device	Predicate
Methodology	Latex enhanced turbidimetry	Fluoroimmunoassay
Controls	Lyophilized human sera with IgE at 2 levels	Human IgE in buffer at 2 levels
Calibrators	Hepes-glycine buffer containing human IgE at 5 different levels.	Human IgE in buffer at 6 levels

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

None referenced.

L. Test Principle:

The Quantia IgE Latex Reagent is a suspension of polystyrene particles of uniform size coated with mouse anti-human IgE monoclonal antibody. When a sample containing IgE is mixed with the latex reagent and the reaction buffer included in the kit, a clear agglutination occurs. The degree of agglutination is directly proportional to the concentration of IgE in the sample and is determined by measuring the decrease of transmitted light caused by the aggregates. Results are expressed in IU/mL of IgE.

M. Performance Characteristics (if/when applicable):

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

      The precision study was performed using three samples (Quantia Ferritin/Myoglobin/IgE low and high controls and a mixture of the two controls), run in duplicate twice a day over 20 days on an AEROSET® System (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	47.3	6.4	2.8	9.4
80	228.4	1.0	0.8	1.5
80	406.5	0.7	0.4	1.0

b. *Linearity/assay reportable range:*
Linearity testing was performed on an AEROSET® System using a serum sample containing 1300 IU/mL of IgE diluted in physiologic saline at 7 different dilutions (5%,10%, 20%,30%, 40%, 50%, and 75%). Each dilution was analyzed in quadruplicate. Testing was done without automatic rerun capability. The reported means were calculated from the pooled results. Regression analysis yielded y = 1.006x – 3.6 and a correlation coefficient (r^2) of 0.9996. Results showed the assay range is linear for IgE concentrations ranging from 25 to 1000 IU/mL.

The AEROSET® System can automatically rerun samples with results above the upper limit of the assay range (1000 IU/mL) at 1:10 sample dilutions and then automatically recalculates the new sample result. Two studies using two sample pools were done to assess the extended linearity range. One sample pool containing 6719 IU/mL IgE was analyzed 4 times the normal sample volume (equivalent to 26,887 IU/mL IgE), was diluted 4 times (6.25%, 12.5%, 25%, and 50%) with physiological saline . The other sample pool containing 3500 IU/mL IgE was analyzed the same way (equivalent to 7812 IU/mL), was diluted 6 times (5%, 10%, 15%, 20%, 30%, and 50%). Each dilution was analyzed in quadruplicate. The reported means were calculated from the pooled results. Regression analysis yielded y= 0.999x + 1.4 and correlation coefficient (r^2) = 0.9880. Results showed that extended assay rangewith automatic rerun capability is linear for IgE concentrations ranging from 25 to 26000 IU/mL.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
The reference material is the 2nd WHO International Reference Preparation Human Serum Immunoglobulin E (IgE), NIBSC code 75/502.Value assignments were determined in multiple runs using specific lots of reagents. A detailed description of the assignment of the Quantia IgE calibrators and control values is provided.

Calibration Stability – The data indicated that the calibration is stable for at least 30 days.

Reconstituted Control Stability – The data indicated that the controls I and II are stable for at least 15 days at 2-8°C after reconstitution.

The shelf-life stability for the standards was 18 months and the controls 24 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 (SD) 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 6.9 IU/mL.

Limit of quantification is the smallest concentration of unknown that can be reliably be quantified by the assay and was determined using 6 dilutions of the 100 IU/mL (10%, 15%, 25%, 33%, 50%, and 75%) Quantia IgE Standard in physiologic saline on an AEROSET® System. Each dilution was run in quadruplicate. The data support the claim for a limit of quantification of 25 IU/mL.

e. *Analytical specificity:*

Interference testing was performed on an AEROSET® System by spiking a sample containing IgE. For each interfering substance, the sample was split into 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 IgE reagent. The acceptance criteria are as follows:

- If the recovery of the spiked sample is within 95-105% of the unspiked sample result (within ± 5%) no further studies are needed. If not, several concentrations of the interfering substances were studied and the concentration causing 5%, 10% and 15% interference were assessed.

No significant interference was observed for:

- Hemoglobin up to 482 mg/dL
- Bilirubin up to 20.8 mg/dL
- Triglycerides up to 1327 mg/dL
- Turbidity of sample up to 2.38 AU/cm at 660 nm.
- Rheumatoid Factor interference is below 10% up to 138 IU/mL.

Since the interference for RF exceeded 5%, a dose response study was performed by mixing in different proportions of the two aliquots. From the fitted interferogram curve, the RF concentrations causing interference was extrapolated with the following results:

5%: 69 IU/mL 10%: 138 IU/mL 15%: 207 IU/mL

No cross-reactivity studies have been conducted with heterophile antibodies and this information is included in the Limitations section of the package insert.

f. Assay cut-off:
Not provided.

2. Comparison studies:
   a. Method comparison with predicate device:
   The table below shows the comparison of 101 serum samples tested with the Quantia IgE on the AEROSET® System and the predicate device Pharmacia UniCap Total IgE. No information about age and gender was provided for the samples used in the study. The sample concentrations covered the entire assay range. The required specifications were: Slope 1.0± 0.20; r = 0.950.

	Aeroset®
Reference Instrument	Uni-CAP 100 (Pharmacia)
Mathematical Method	Linear Regression
Slope	0.9650
95% CI	0.9211 to 0.9831
Intercept (IU/mL)	-17.443
95% CI	-40.296 to 5.4111
Range (IU/mL)	10 – 2269
Mean X (IU/mL)	350.3
Mean Y (IU/mL)	310.9
R	0.9750
S_{YX}	87.6
n	101

   b. Matrix comparison:
   Fifty-two sets of paired plasma and serum samples were run. The plasma samples were from Sodium EDTA, potassium EDTA, Sodium Heparin, lithium heparin and Citrate. The linear regression statistics are shown below.

	Na-EDTA	**K-EDTA**	**Na-Heparin**	**Li-Heparin**	**Citric acid**
Slope	0.968 (95% CI: 0.963 to 0.973)	0.982 (95% CI: 0.976 to 0.989)	0.978 (95% CI: 0.973 to 0.983)	0.978 (95% CI: 0.973 to 0.983)	0.963 (95% CI: 0.955 to 0.972)
y Intercept	-1.553 (95% CI: -3.099 to -0.007)	-1.878 (95% CI: -3.873 to 0.117)	-0.462 (95% CI: -1.983 to 1.060)	-1.272 (95% CI: -2.761 to 0.218)	-2.226 (95% CI: -4.702 to 0.250)
Correlation	0.9998	0.9997	0.9998	0.9998	0.9995

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 IgE is from a literature: In clinically healthy subjects the serum IgE levels exhibit a wide distribution range and do not follow a normal distribution. Age related concentrations must be taken into account when interpreting IgE values in children. IgE does not cross the placental barrier so IgE is not detectable in newborn. The IgE concentration increases during the first years of life, reaching a peak at 10-15 years and dropping subsequently to adult values[1]. As the limit of quantification of Quantia IgE is 25 IU/mL, it is not recommended to use this test with children below the age of 12 months.

Age	Neonates	1-12 mos	1-5 yrs	6-9 yrs	10-15 yrs	Adults
Concentration (IU/mL)	<1.5	<15	<60	<90	<200	<100

1. Ringel KP, Dati F, Buchholz, E. IgE-Normalwerte bei Kindem. Laboratoriumsblatter 32,26-34, 1982

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.