

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

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

k052819

**B. Purpose for Submission:**

This is a new device.

**C. Measurand:**

Alpha-1 Antitrypsin

**D. Type of Test:**

Quantitative immunoturbidimetric assay

**E. Applicant:**

Ortho-Clinical Diagnostics, Inc.

**F. Proprietary and Established Names:**

VITROS Chemistry Products AAT Reagent

VITROS Chemistry Products Calibrator Kit 99

VITROS Chemistry Products AAT Performance Verifiers I, II, and III

**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)

JIX, Calibrator, Multi-Analyte Mixture

4. Panel:

Immunology (82)

Chemistry (75)

**H. Intended Use:**

1. Intended use(s):

VITROS Chemistry Products AAT Reagent is used to quantitatively measure  $\alpha$ 1- antitrypsin concentration in human serum. The measurement of  $\alpha$ 1- antitrypsin in serum aids in the diagnosis of cirrhosis of the liver and pulmonary emphysema.

VITROS Chemistry Products Calibrator Kit 99 is used to calibrate VITROS 5, 1 FS Chemistry systems for the quantitative measurement of  $\alpha$ 1- Antitrypsin (AAT).

VITROS Chemistry Products AAT Performance Verifiers are assayed controls used to monitor performance of VITROS AAT Reagents on

- VITROS 5, 1 FS Chemistry systems.
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 VITROS 5, 1 FS Chemistry systems (k031924).

**I. Device Description:**

The VITROS Chemistry Products AAT Reagent is used in conjunction with the VITROS Chemistry Products Calibrator Kit 99 and VITROS Chemistry Products FS Diluent Pack 2 (BSA/Saline) on VITROS 5, 1 FS Chemistry Systems. The VITROS is a dual chambered package containing ready to use liquid reagents: Reagent 1 buffer containing a polymer, and Reagent 2 containing goat antisera to human alpha 1-antitrypsin.

The VITROS Chemistry Products Calibrator Kit 99 is prepared from processed human serum to which inorganic salts, buffers, and preservatives have been added. These standards are used to calibrate VITROS 5, 1 FS Chemistry Systems for the quantitative measurement of AAT. They consist of 5 levels ranging in concentration from 36 to 360 mg/dL.

The VITROS Chemistry Products AAT Performance Verifiers I, II, and III are prepared from processed human serum to which inorganic salts, buffers, and preservatives have been added. These are assayed controls used to monitor the performance of VITROS Chemistry Products AAT Reagent on VITROS 5, 1 FS Chemistry Systems.

The controls and standards are sold separately.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):  
IMMAGE® Immunochemistry Systems AAT Reagent  
IMMAGE® Immunochemistry Systems Calibrator 2  
VITROS Chemistry Products Protein Performance Verifiers
2. Predicate 510(k) number(s):  
k964766  
k973932  
k042477
3. Comparison with predicate:

<b>Similarities</b>		
Item	Device	Predicate
	<b>VITROS AAT Assay</b>	<b>IMMAGE AAT Assay</b>
Intended Use	Quantitative in vitro diagnostic determination of alpha 1-antitrypsin	Same
Sample type	Serum	Same

Similarities		
Item	Device	Predicate
Antibody source	Goat	Same
Matrix	Performance verifiers prepared from processed human serum to which salts, buffers and preservatives have been added	Same
Components	Controls and standards are sold separately.	Same

Differences		
Item	Device	Predicate
Methodology	Immunoturbidimetry	Nephelometry
Calibrator levels	Five levels	Single level
Calibrator format	Liquid	Lyophilized
Standardization	BAM-IRMM-LGC (Institute for reference Methods and Materials/Laboratory of the Gov't Chemist) ERM-DA 470	International Reference Preparation for Plasma Proteins CRM 470
QC Material	VITROS AAT Performance verifiers	Two levels of any control material

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

None referenced.

**L. Test Principle:**

The VITROS AAT Reagent is a dual chambered package containing ready to use liquids. Samples, calibrators, and controls are automatically diluted in saline from VITROS FS Diluent Pack 2 and mixed with Reagent 1 containing a polymer. Addition of antisera specific for human alpha 1-antitrypsin (Reagent 2) produces an immunochemical reaction yielding antigen/antibody complexes. The light scattering properties of the antigen/antibody complexes increase solution turbidity proportional to AAT concentration in the sample. The turbidity is measured spectrophotometrically at 340nm. Once a calibration has been performed for each reagent lot, the AAT concentration in each unknown sample can be determined using the sorted calibration curve and the measured absorbance obtained in the assay of the sample

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

1. Analytical performance:

a. *Precision/Reproducibility:*

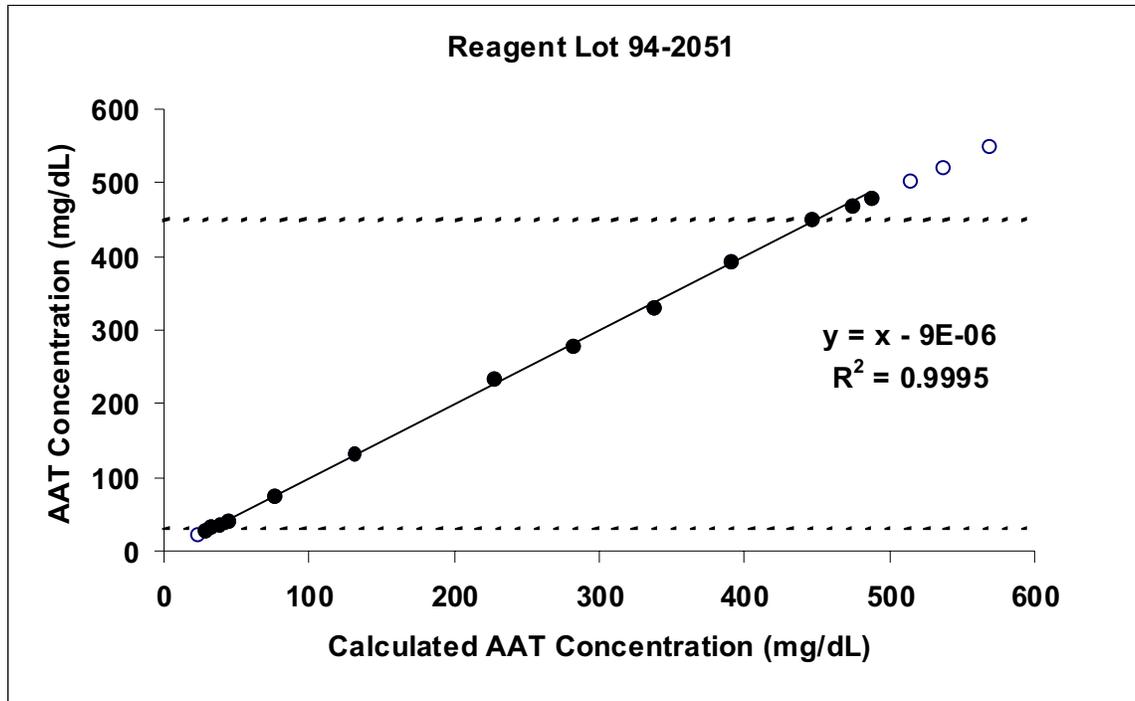
Within-Day precision was determined using two runs per day with 2 replicates per run. Runs within-day were separated by at least two hours. Within-Lab precision was determined using a single lot of reagents with

one analyzer and four calibrators.  
 Additional testing around the low end of the analytical range was performed with 6 replicates per run for 3 days.

N	Mean (mg/dL)	Within Day %CV	Within Lab %CV	No. of days	Reps per run
18	36.08	1.47	3.16	3	6
18	37.56	2.66	2.66	3	6
18	29.98	1.07	2.67	3	6
88	53.22	1.11	3.06	22	2
88	114.75	1.18	1.34	22	2
88	262.98	1.44	3.07	22	2
88	387.29	1.82	2.90	22	2

b. *Linearity/assay reportable range:*

Linearity testing was performed by comparison of the measured with calculated analyte concentration of mixed pools, prepared at concentrations covering the entire assay range. The low pool had an estimated concentration of 25.8 mg/dL. The high pool had an estimated concentration of 499.6 mg/dL. Fifteen levels spanning the assay reportable range were created. Four determinations of each level and each of the three AAT Performance Verifiers were made. Results are shown below. Linearity was set at 30 to 450 mg/dL.



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

The values assigned to the VITROS Chemistry Products Calibrator Kit 99 for AAT are traceable to BAM-IRMM-LGC (Bundesanstalt für Materialforschung und-prüfung/Institute for Reference Methods and Materials/Laboratory of the Gov't Chemist) ERM-DA 470 Reference Material. A five level set of calibrators are prepared and are used to calibrate the Master Lot which is used to assign values to new product lots of the VITROS Chemistry Products AAT Reagent and VITROS Chemistry Products Calibrator Kit 99.

Control values are assigned by running five VITROS Chemistry Systems in five different laboratories. Data was collected over 10 days, 2 runs/day and 2 replicates per run for each performance verifier.

Calibrator Kit Stability – Unopened kit are stable for six months when stored refrigerated at 2°-8°C. Opened vials are stable at ≤3 days when stored capped between 2-8°C.

Performance Verifiers Stability – Unopened kit are stable for six months when stored refrigerated at 2°-8°C. The stability of opened vials stored capped between 2°-8°C is up to 4 weeks.

d. *Detection limit:*

Detection limit was calculated by running 3 AAT samples with concentrations of 13.1, 15.0, and 16.9 mg/dL. LOD was determined for three reagent lots, run twice per day with 5 replicates per run over 3 days on two VITROS Chemistry systems for a total of 60 replicates. The mean and the standard deviation were calculated. The Detection Limit was found to be 17.3 mg/dL.

The lower end of the linear range was used to determine Limit of quantitation since the limit of detection was determined to be less than the low end of the linear range for all three lots. A limit of quantification is the smallest concentration of unknown that can be reliably be quantified by the instrumental method. The limit of quantitation is established at 30.0 mg/dL.

e. *Analytical specificity:*

Interference: The substances listed below at the concentrations shown were tested and found not to interfere.

**Substances Tested that do not Interfere**

<b>Compound</b>	<b>Concentration</b>
Acetaminophen	20 mg/dL
Acetyl-L-cysteine	100 mg/dL
Amoxicillin	20ug/mL
Ascorbic acid (L)	3 mg/dL
Bilirubin	60 mg/dL
Carbamazepine	120 ug/mL
Dipyron	30 mg/dL
B-Estradiol	2.7 mg/dL
Ethamsylate	3 mg/dL
Gentamicin sulfate	120 ug/mL
Hemoglobin	1000 mg/dL

Compound	Concentration
Ibuprofen	400 ug/mL
Intralipid	500 mg/dL
Lidocaine	60 ug/mL
Methotrexate	90.9 mg/dL
Procainamide	100 ug/mL
Propranolol	5 ug/mL
Rantidine	200 ug/mL
Salicylic acid	50 mg/dL
Simvastatin	16 ug/mL
Theophylline	25 mg/dL
Triglyceride	1000 mg/dL
Valproic acid	500 ug/mL

f. *Assay cut-off:*  
Not provided.

2. Comparison studies:

a. *Method comparison with predicate device:*

A total of 175 human serum samples were assayed using the VITROS AAT assay and its predicate device, IMAGE AAT assay. Each sample was measured in duplicate on each system. Testing was performed with two lots of VITROS AAT reagents on two VITROS 5, 1 FS Chemistry Systems. There were 97 female patient samples whose age ranged from 23 to 58 years. There were 77 male patient samples whose age ranged from 3 months to 66 years. The results are shown below.

VITROS AAT vs. IMAGE AAT	
Slope	0.9262 (95% CI: 0.906 to 0.952)
Intercept	2.064 (95% CI: -1.698 to 5.37)
Range (mg/dL)	30.0 to 450
r	0.996
N	175

b. *Matrix comparison:*

Serum is the only recommended matrix for this device

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:

Reference intervals were determined by testing 145 random specimens from healthy adult subjects. Testing was performed on two VITROS 5, 1 FS

Chemistry systems. The reference interval based on the study was determined to be 88 to 183 mg/dL.

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.