510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:
k071525

B. Purpose for Submission:
Clearance of new device and FlexRate Method for this device

C. Measurand:
Aspartate aminotransferase (AST/SGOT)

D. Type of Test:
Quantitative enzymatic assay

E. Applicant:
Abbott Laboratories

F. Proprietary and Established Names:
Activated Aspartate Aminotransferase

G. Regulatory Information:
1. Regulation section:
   21 CFR 862.1100
2. Classification:
   Class II
3. Product code:
   CIT
4. Panel:
   Chemistry (75)

H. Intended Use:
1. Intended use(s):
   See Indication for use below.
2. Indication(s) for use:
   Activated Aspartate Aminotransferase (AST/SGOT) test system is a device intended to measure the activity of the enzyme aspartate aminotransferase (AST) (also known as a serum glutamic oxaloacetic transferase or SGOT) in serum and plasma. Aspartate Aminotransferase measurements are used in the diagnosis and treatment of certain types of liver and heart disease.
3. Special conditions for use statement(s):
   For prescription use only.
4. Special instrument requirements:
   For use with the Abbott AEROSET and ARCHITECT *c*Systems.

I. Device Description:

The kit is compromised of two ready-to-use liquid reagents. R1 contains *L*-aspartic acid, β-NADH, LD, MDH, pyridoxal phosphate monohydrate and buffer. R2 contains *L*-aspartic acid, 2-oxoglutaric acid and buffer.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Abbott Clinical Chemistry Aspartate Aminotransferase Activated assay
2. Predicate 510(k) number(s):
   k981221
3. Comparison with predicate:

Differences		
Characteristic	Predicate device (k981221)	Proposed device
Reagent format	Lyophilized reagent requiring reconstitution prior to use	Liquid ready-to-use reagent
Limit of Quantitation	9 U/L	5 U/L

Similarities		
Characteristic	Predicate device (k981221)	Proposed device
Intended use	The Abbott Activated Aspartate Aminotransferase assay is used for the quantitation of aspartate aminotransferase (also known as serum glutamic oxaloacetic transferase or SGOT) in human serum or plasma.	Same
Test principle	The assay is a clinical chemistry assay in which the aspartate aminotransferase catalyzes the transfer of the amino group from *L*-aspartate to α-ketoglutarate, in the presence of pyridoxal-5'-phosphate, forming oxaloacetate and *L*-glutamate. Oxaloacetate in the presence of NADH and malate dehydrogenase (MDH) is reduced to *L*-malate. In this reaction, the	Same

	NADH is concomitantly oxidized to NAD. The reaction is monitored by measuring the rate of decrease in absorbance at 340 nm due to the oxidation of NADH to NAD.	
Sample matrix	Serum or plasma	Same
Recommended diluent	Saline	Same

K. Standard/Guidance Documents Referenced (if applicable):
  • *User Evaluation of Precision Performance of Clinical Chemistry Devices: Approved Guideline* (EP5-A2)
  • *Evaluation of the Linearity of Quantitative Measurement Procedures: a Statistical Approach: Approved Guideline* (EP6-A2)
  • *Interference Testing in Clinical Chemistry: Approved Guideline* (EP7-A2)
  • *Method Comparison and Bias Estimation using Patient Samples: Approved Guideline* (EP9-A2)
  • *Protocols for Determination of Limits of Detection and Limits of Quantitation* (EP17-A3)

L. Test Principle:
The Activated Aspartate Aminotransferase (AST) assay is a clinical chemistry assay in which the aspartate aminotransferase catalyzes the transfer of the amino group from *L*-aspartate to α-ketoglutarate, in the presence of pyridoxal-5'-phosphate, forming oxaloacetate and *L*-glutamate. Oxaloacetate in the presence of NADH and malate dehydrogenase (MDH) is reduced to *L*-malate. In this reaction the NADH is concomitantly oxidized to NAD. The reaction is monitored by measuring the rate of decrease in absorbance at 340 nm due to the oxidation of NADH to NAD.

M. Performance Characteristics (if/when applicable):
  1. Analytical performance:
    a. *Precision/Reproducibility:*
       Precision studies were performed using CLSI Document EP5-A as a guideline. The total precision as well as the precision for each component of variation (between-day, between-run, and within-run) was evaluated for AST. On one *c*8000 instrument, four control levels (two at normal, two at abnormal analyte concentrations) were tested; the high test sample was within the FlexRate Method range. On the remaining instruments, two control levels at normal and abnormal analyte concentrations were tested. A five-day precision study for the Activated AST assay was run on three *c*8000 systems, one AEROSET System and one *c*16000 System. Testing consisted of two runs per day, five replicates per run (a total of 50 data points). Samples used were either commercial control material, normal serum pool or spiked serum pool.

Initial precision testing demonstrated that results were equivalent across the platforms, so one full 20-day protocol was continued on 3 *c*8000 Systems, two runs per day, two replicates per run, two control levels only (a total of 80 data points on each instrument tested).

*c*8000; Instrument 1:

Control		Level 1	Level 2	Level 3	Level 4
N		80	80	50	50
Mean (U/L)		42.22	192.50	22.9	3436.7
Within Run	SD	1.06	1.16	0.41	15.32
	%CV	2.50	0.60	1.8	0.5
Between Run	SD	0.00	0.92	0.39	11.02
	%CV	0.00	0.48	1.7	0.3
Between Day	SD	1.56	1.25	00.00	16.30
	%CV	3.71	0.65	0.0	0.5
Total	SD	1.89	1.93	0.56	24.93
	%CV	4.47	1.00	2.4	0.7

*c*8000; Instrument 2:

Control		Level 1	Level 2
N		80	80
Mean (U/L)		42.27	192.44
Within Run	SD	0.50	0.75
	%CV	1.17	0.39
Between Run	SD	0.29	0.87
	%CV	0.68	0.45
Between Day	SD	0.91	0.86
	%CV	2.16	0.45
Total	SD	1.08	1.43
	%CV	2.55	0.75

*c*8000; Instrument 3:

Control		Level 1	Level 2
N		80	80
Mean (U/L)		42.68	191.65
Within Run	SD	0.55	0.79
	%CV	1.29	0.41
Between Run	SD	0.38	1.17
	%CV	0.89	0.61
Between Day	SD	1.13	0.72
	%CV	2.66	0.38
Total	SD	1.32	1.59
	%CV	3.08	0.83

AEROSET (5 day precision study):

Control		Level 1	Level 2
N		50	50
Mean (U/L)		46.16	205.15
Within Run	SD	0.63	1.17
	%CV	1.36	0.57
Between Run	SD	0.83	0.89
	%CV	1.79	0.43
Between Day	SD	0.00	0.00
	%CV	0.00	0.00
Total	SD	1.04	1.47
	%CV	2.25	0.72

*c*16000 (5 day precision study):

Control		Level 1	Level 2
N		50	50
Mean (U/L)		44.60	196.60
Within Run	SD	0.50	0.51
	%CV	1.12	0.26
Between Run	SD	0.15	0.90
	%CV	0.33	0.46
Between Day	SD	0.60	0.00
	%CV	1.34	0.00
Total	SD	0.79	1.04
	%CV	1.78	0.53

b. *Linearity/assay reportable range:*
   To establish the linearity of the assay, a study design was used based on CLSI protocol EP6-A: *Evaluation of the Linearity of Quantitative Measurement Procedures: a Statistical Approach: Approved Guideline.*
   The claimed measuring range for this assay is 5 - 1,985 U/L on all three instruments, extending up to 5,364 U/L using FlexRate linearity. A serum pool with very low AST was spiked with commercially available AST to obtain the high AST sample then diluted with saline (the recommended diluent). A minimum of nine samples at concentrations spanning the claimed linear range of the assay (5 – 5400 U/L) were run in a minimum of four replicates. The assay recovery was within ± 10% or ± 8 U/L of the expected result at all tested concentrations.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
   The shelf-life and on board stability testing protocols for the AST reagent and the acceptance criteria were described and found to be acceptable.

d. *Detection limit:*
   To determine the limit of detection (LoD) and limit of quantitation (LoQ), a study design was used based on CLSI protocol EP17-A: *Protocols for Determination of Limits of Detection and Limits of Quantitation*.
   Twenty replicates of two low AST samples were run on three instruments each of the AEROSET system, a *c*8000 and a *c*16000. To determine the LoQ, test levels near the linear low for the AST Activated assay were run in replicates of 10, on three instruments, two runs per instrument.
   Conclusions: The LoD was calculated to be 3.8 U/L. The Limit of Quantitation (LoQ) was calculated to be 5 U/L and was defined as the concentration of the analyte demonstrated imprecision less than or equal to 20% CV.

Limit of Detection:

	Instrument	N	Limit of Blank (U/L)	SD	Limit of Detection (U/L)
AEROSET	1	20	1.2153	1.5542	3.8061
	2	20	1.3608	0.6278	2.3936
	3	20	1.7525	0.7124	2.9243
ARCHITECT c8000	1	20	1.9388	0.3890	2.5788
	2	20	0.6057	0.4535	1.3617
	3	20	2.1067	0.3440	2.6725
ARCHITECT c16000	1	20	0.3333	0.2614	0.7633
	2	20	0.5911	0.3099	1.1008
	3	20	0.5476	0.2556	0.9737

Limit of Quantitation – AEROSET:

| Instrument | Level | N | Mean (U/L) | Imprecision | |
				SD	%CV
1	1	20	1.8550	0.6278	33.8459
	2	20	4.0200	0.6263	15.5788
	3	20	5.5000	0.6497	11.8127
	4	20	8.1750	0.6904	8.4458
	5	20	10.3900	0.7663	7.3757
2	1	20	2.4700	0.7124	28.8410
	2	20	4.4600	0.4773	10.7012
	3	20	6.2750	0.8168	13.0175
	4	20	8.3450	0.8757	10.4935
	5	20	10.9550	0.7104	6.4850
3	1	20	2.7100	1.5542	57.3523
	2	20	3.4050	0.4371	12.8360
	3	20	5.3200	0.6510	12.2367
	4	20	8.3250	0.9867	11.8521
	5	20	10.1350	0.6706	6.6171

Limit of Quantification – ARCHITECT *c*8000:

				Imprecision	
Instrument	Level	N	Mean (U/L)	SD	%CV
1	1	20	1.1947	0.4523	37.8598
	2	20	2.6342	0.3890	14.7690
	3	20	4.8656	0.3735	7.6765
	4	20	6.1353	0.5065	8.2558
	5	20	8.7782	0.4136	4.7121
2	1	20	2.0109	0.4535	22.5506
	2	20	2.8796	0.2698	9.361
	3	20	4.8181	0.3153	6.5435
	4	20	7.3387	0.4431	6.0383
	5	20	9.1173	0.5267	5.7774
3	1	20	1.0598	0.6364	60.0485
	2	20	2.7560	0.3440	12.4812
	3	20	4.5546	0.6079	13.3472
	4	20	6.2458	0.5049	8.0840
	5	20	8.6508	0.6308	7.2920

Limit of Quantification - ARCHITECT *c*16000

Instrument	Level	N	Mean (U/L)	Imprecision	
				SD	%CV
1	1	20	1.2041	0.3099	25.7333
	2	20	2.8260	0.4546	16.0869
	3	20	4.7882	0.4279	8.9357
	4	20	7.6416	0.3962	5.1848
	5	20	9.6700	0.4361	4.5101
2	1	20	1.9579	0.2556	13.0562
	2	20	3.9950	0.2565	6.4203
	3	20	5.6307	0.3209	5.6991
	4	20	8.2524	0.4829	5.8519
	5	20	10.57	0.2758	2.6072
3	1	20	–0.0530	0.2026	–381.935
	2	20	2.1490	0.2614	12.1647
	3	20	3.9513	0.2796	7.0760
	4	20	5.7156	0.2446	4.2796
	5	20	8.8245	0.2871	3.253

e. *Analytical specificity:*
Human serum samples at the clinical decision point of the analyte were spiked with various levels of interferents. A minimum of four replicates of each interferent level and four replicates of reference sample were run. The percent recovery was determined by dividing the mean result of each interferent sample by the mean result of the reference sample. The level of interference was considered acceptable if there was no more than ± 10% difference between the interferent result and the reference result. Testing was performed using the ARCHITECT *c*8000.

The percent interference was within ± 10% difference for serum samples containing up to 60 mg/dL bilirubin; 62 mg/dL hemoglobin; and 500 mg/dL Intralipid at the clinical decision point.

The sponsor did not test other commonly used medications and other endogenous substances and referred the user to literature for other interferences known to affect AST assays.

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

2. <u>Comparison studies:</u>
a. *Method comparison with predicate device:*
The Abbott Activated AST assay was compared to the predicate device using CLSI Document EP9-A2 as a guideline for the method comparison study. Note: any samples with AST concentrations above 993 U/L were diluted prior to testing on the predicate, but were undiluted when testing with the proposed device.

AEROSET: to evaluate the proposed device (Activated AST on the AEROSET) vs. the predicate device (AST Activated on the Abbott AEROSET (k981221), 104 clinical serum and plasma samples and 26 spiked serum samples ranging from 14-4993 U/L were tested.
Correlation coefficient = 0.999
Slope = 1.06
y-intercept = -3.79 U/L

ARCHITECT *c*8000 system: To evaluate the performance of the proposed device (Activated AST) vs. the predicate device (AST Activated on the Abbott AEROSET (k981221), 104 clinical serum and plasma samples and 26 spiked serum samples ranging from 14 – 4993 U/L were tested.
Correlation coefficient= 0.999
Slope = 1.01
y-intercept = -4.15 U/L.

ARCHITECT *c*16000 system: To evaluate the performance of the proposed device (Activated AST on the ARCHITECT *c*16000) vs. the predicate device (AST Activated on the Abbott AEROSET (k981221), 104 clinical serum and plasma samples and 26 spiked serum samples ranging from 14 – 4993 U/L were tested.
Correlation coefficient= 0.999
Slope = 1.03
y-intercept = -3.75 U/L.

   b. *Matrix comparison:*
   Blood was drawn from 37 subjects, some samples were spiked with various concentrations of AST to achieve samples that spanned the entire measuring range (17 – 5000 U/L), and processed to produce a full set of matched specimen types (serum, lithium heparin plasma, sodium heparin plasma, EDTA plasma, plasma gel tube (PST) and serum gel tube (SST)). The percent difference seen when using other sample types compared to serum was within ± 10% for all samples tested.

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 stated reference range for AST in serum and plasma of 5 – 34 U/L in adults[1] is based on published literature. The sponsor recommends that each laboratory determine its own reference range based on its particular locale and population characteristics.

   [1] Kazmierczak SC. Aspartate aminotransferase. In: Kaplan LA, Pesce A, editors. *Clinical Chemistry Theory, Analysis and Correlation*, 3rd ed. St. Louis, MO: CV Mosby; 1196:523.

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.