

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

A. 510(k) Number:

k071580

B. Purpose for Submission:

New device

C. Measurand:

Aspartate Amino Transferase (AST/GOT)

D. Type of Test:

Quantitative enzymatic assay

E. Applicant:

Thermo Fisher Scientific

F. Proprietary and Established Names:

AST/GOT (IFCC)

eCal, code 981830

Nortrol, code 981043

Abtrol, code 981044

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
NADH oxidation/NAD reduction, AST/SGOT (CIT)	Class II	21 CFR 862.1100 Aspartate amino transferase (AST/SGOT) test system	75 Clinical Chemistry(CH)
Product Code	Classification	Regulation Section	Panel
Calibrator, Multi-Analyte Mixture (JIX)	Class II	21 CFR 862.1150 Calibrator	75 Clinical Chemistry(CH)
Product Code	Classification	Regulation Section	Panel
Multi-analyte controls, all kinds (assayed and unassayed) (JJY)	Class I	21 CFR§ 862.1660 Quality control material (assayed and unassayed)	75 Clinical Chemistry(CH)

H. Intended Use:

1. Intended use(s):

See Indications for use below.

2. Indication(s) for use:

AST / GOT (IFCC)

The AST/ GOT (IFCC) test system is intended for quantitative *in-vitro* diagnostic determination of the activity of the enzyme aspartate amino transferase (AST) (also known as a serum glutamic oxaloacetic transferase or SGOT) in serum and plasma on T60 instrument. Measurement of aspartate amino transferase levels aids in the diagnosis and treatment of certain types of liver and heart disease.

Auxiliary product: Pyridoxal Phosphate

Auxiliary reagent for in vitro diagnostic use in the quantitative determination of AST (GOT) codes 981363 and 981771, activity according to the IFCC recommendations with 3-reagent method on T60 instrument.

eCal

For in vitro diagnostic use on T60 instrument. eCal is used as a calibrator for enzyme tests using methods defined by Thermo Fisher Scientific Oy

Nortrol

For *in vitro* diagnostic use for quantitative testing on T60 instrument. Nortrol is a control serum to monitor precision of the analytes listed in the separate Nortrol value sheet. The given values are valid for T60 Clinical Chemistry Instruments using methods defined by Thermo Fisher Scientific Oy.

Abtrol

For *in vitro* diagnostic use for quantitative testing on T60 instrument. Abtrol is a control serum to monitor precision of the analytes listed in the separate Abtrol value sheet. The given values are valid for T60 Clinical Chemistry Instruments using methods defined by Thermo Fisher Scientific Oy.

3. Special conditions for use statement(s):

For Prescription use only

4. Special instrument requirements:

To be used with T60 chemistry analyzer systems.

I. Device Description:

The device is supplied as ready-to-use, IVD reagent kit with reagent A and reagent B. A third optional reagent, available separately is pyridoxal-5'-phosphate which is needed for the 3-reagent method. For the one-reagent method, the entire contents of reagent B are added to reagent A and are mixed well before use. For the three reagent method, reagent A, reagent B and pyridoxal-5'-phosphate are not mixed together.

Reagent A (Enzyme reagent) contains Tris buffer, pH 7.8 (110 mmol/L), L-Aspartate (325 mmol/L), LDH (> 810 U/L) MDH (> 810 U/L), NaN (< 0.1 %).

Reagent B (substrate) contains 2-Oxoglutarate (65 mmol/L), NADH (1.0 mmol/L), NaN (< 0.1 %).

Liquid pyridoxal-5'-phosphate which is supplied separately is needed for the 3-reagent method.

All human materials included in the calibrators and controls were tested by FDA approved methods and found to be negative for the presence of antibodies to HIV-1, HIV-2, HBsAg, and HCV.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Bayer ADVIA IMS Aspartate Aminotransferase (AST)
2. Predicate 510(k) number(s):
k992136
3. Comparison with predicate:

Characteristics	New Device (k071580)	Bayer ADVIA IMS Aspartate Aminotransferase (AST) (k992136)
Indications for Use	The AST/ GOT (IFCC) test system is intended for quantitative <i>in-vitro</i> diagnostic determination of the activity of the enzyme aspartate amino transferase (AST) (also known as a serum glutamic oxaloacetic transferase or SGOT) in serum and plasma on T60 instrument. Measurement of aspartate amino transferase levels aids in the diagnosis and treatment of certain types of liver and heart disease.	For in vitro diagnostic use in the quantitative determination of aspartate amino transferase activity in human serum and plasma on the ADVIA Chemistry systems. Such measurements are used mainly to determine the progress and prognosis of patients with myocardial infarction and the diagnosis and monitoring of liver disease.
Assay protocol	1-reagent method: Modified IFCC reference method (without PyP) 3-reagent method: IFCC reference method	1-reagent method: Modified IFCC 3-reagent method: IFCC
Sample type	Serum, plasma (heparin)	Serum, plasma (Li-heparin)
Traceability	1-reagent method is traceable to molar absorbance coefficient of NADH 3-reagent method traceable to IFCC reference method	1-reagent method and 3-reagent method is traceable to IFCC
Format	Reagent provided as a ready to use liquid.	Reagent is provided in a ready to use format.
Storage/Stability	Reagent in unopened vial is stable at 2-8°C until expiration date on vial label when protected from light.	Shelf life at 2-8°C until the expiration date on the label.
Expected values	Male: <35 U/L; Female: <31 U/L	1-reagent method: <34 U/L 3-reagent method: 13-40 U/L

Linearity/Assay range	1-reagent method: 4 – 350 U/L 3-reagent method: 4 – 300 U/L	0 – 1000 U/L
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K. Standard/Guidance Document Referenced (if applicable):

CLSI EP5-A: Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline. Vol. 19 No.2. February 1999.

CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline Vol. 23 No.16. April 2003.

CLSI EP7-A: Interference Testing in Clinical Chemistry: Approved Guideline Vol. 22 No.27. December 2002.

CLSI EP9-A: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline. Vol. 15 No. 17. December 1995.

L. Test Principle:

AST catalyses the transfer of amino group from aspartate to oxoglutarate during the formation of glutamate and oxaloacetate. Oxaloacetate is reduced to malate by malate dehydrogenase (MDH). During this conversion, an equivalent amount of NADH is oxidized to NAD. The resulting decrease in absorbance at 340 nm is directly proportional to the activity of AST in serum.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Following CLSI EP5-A, the sponsor evaluated the precision using two lots of reagents and three levels of commercially available serum controls on T60 analyzer. Studies were carried out in duplicates of two runs per day over 20 days (total of 80 data points). The results are tabulated below.

One-reagent method:

	Mean (38 U/L)		Mean (101 U/L)		Mean (189 U/L)	
	SD	CV%	SD	CV%	SD	CV%
Within run	0.5	1.4	0.9	0.9	1.0	0.5
Between run	-	-	0.5	0.5	1.1	0.6
Total	0.9	2.4	2.0	2.0	3.2	1.7

Three-reagent method:

	Mean (38 U/L)		Mean (101 U/L)		Mean (189 U/L)	
	SD	CV%	SD	CV%	SD	CV%
Within run	0.6	1.5	1.3	1.1	1.0	0.5
Between run	0.4	1.0	1.4	1.1	1.2	0.6
Total	1.0	2.7	2.5	2.0	2.9	1.5

b. Linearity/assay reportable range:

Following instructions in CLSI Document EP6-A, the sponsor conducted separate studies on T60 instrument for 1-reagent and 3-reagent methods using

different samples to determine the linearity. For 1-reagent method, the sample panel with eight analyte levels, Document Enzyme Linearity Test Set E100 (0 – 384 U/L), was used and four parallel measurements were made at each level. Based on the acceptance criteria $\pm 10\%$ and one of four measurements out of specification acceptable, the sponsor claimed assay range of 4 – 350 U/L for 1-reagent method. For the 3-reagent method, the sponsor used normal human sera spiked with commercially available AST preparation and made 11 analyte levels (5 – 380 U/L) for testing. Each analyte was measured four times. Based on the same acceptance criterion in 1-reagent method and based on the limit of blank (LOB) described below as 2 U/L, the sponsor claimed measuring range of 4 – 300 U/L for 3-reagent method.

To demonstrate the extended measurement range, the sponsor used normal human sera spiked with AST enzyme preparation and made ten dilution steps from the highest concentration down to normal human sera. With maximum allowable bias of $\pm 10\%$ from the estimated straight line, the sponsor claimed extended range of 4 – 2100 U/L for 1-reagent and 4 – 1800 U/L for 3-reagent methods.

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

The sponsor's protocols indicate that calibrator (eCal) is traceable to the reference procedure given in the value sheet, which is IFCC reference procedure for 3-reagent method and molar absorbance coefficient of NADH for 1-reagent method. The controls (Nortrol and Abtrol) are traceable to the IFCC procedure. The values are lot-specific and are assigned based on multi determinations performed using several T60 instruments. The assigned value is the median of all the values generated for each calibrator and control. Additionally, control range is calculated as the target value ± 2 standard deviations. Please refer to the value assignment sheet in the labeling for lot-specific values.

To ensure adequate quality control, the sponsor recommends calibrating the test at least every three days and every time a new reagent bottle is used. The sponsor also recommends using quality control samples at least once a day, after each calibration and when a new bottle is used. However, the sponsor also suggests the control intervals must be adapted to the individual laboratory requirement.

The sponsor claims that all open on-board stability for reagents is 14 days. Reagent in unopened vial is stable at 2-8°C until expiration date on vial label when protected from light.

d. Limit of Detection:

To demonstrate the lower limit of the assay range, the sponsor used a 0.9% Sodium Chloride solution (blank sample) and tested in 20 replicates. The sponsor defined the limit of zero-concentration (Limit Of Blank) sample as $+3SD$, which was demonstrated to be 1.425 U/L for 1-reagent method and 1.73 U/L for 3-reagent method. Based on this information, the sponsor claimed 2 U/L as the lower limit of the detection.

e. Analytical specificity:

Following instructions in CLSI document EP7-A, the sponsor evaluated the effect of known endogenous interferents. The interferents and the test range included hemoglobin (0 – 250 mg/dL), Lipemia (0 – 200 mg/dL), and bilirubin (conjugated and unconjugated). Three levels of analyte concentrations were used: low level sample using normal human sera (1-reagent method) or normal human sera diluted with 0.9% NaCl (3-reagent method); medium level sample from normal human sera spiked with AST enzyme preparation; high level sample from normal human sera spiked with AST enzyme preparation. Interference studies were conducted for both 1-reagent and 3-reagent assay formats. Based on the acceptance criteria of $\pm 10\%$ or ± 2.5 U/L of control (non-interfered) value, the sponsor claimed for both 1-reagent and 3-reagent method, no interference for Lipemia up to 150 mg/dL. For bilirubin (conjugated and unconjugated), no interference were demonstrated for 1-reagent method up to 35 mg/dL, and 3-reagent method up to 58 mg/dL. The results of hemolysate studies demonstrated interference for hemolysate concentrations as low as 46 mg/dL for 1-reagent and 31 mg/dL for 3-reagent methods, depending on the analyte (AST) concentration. Thus, the sponsor recommends not using hemolyzed samples.

f. Assay cut-off:

Not Applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Performance of the AST (IFCC) 1-reagent and 3-reagent methods on T60 analyzer was compared with the results generated for the predicate device, Bayer ADVIA IMS Aspartate Aminotransferase on ADVIA 1650 instrument using 85 serum samples. The samples were split and run on both devices in duplicates. Comparison of data based on predicate and the device produced correlation coefficients (r) of 0.992 and 0.994 for 1-reagent and 3-reagent methods, respectively. Deming regression analysis for 1-reagent and 3-reagent methods resulted in the equations, $y = 0.95x - 2.0$ and $y = 0.94x + 1.3$, respectively. Sample measurement range for 1-reagent method was 12 – 307 U/L and 3-reagent method was 15 – 408 U/L. Based on the sponsor's acceptance criteria of $r \geq 0.9$, the method comparison demonstrated substantial equivalence of the new device to the predicate.

b. Matrix comparison:

The sponsor conducted matrix comparison studies using 45 matched serum and plasma samples for both 1-reagent (sample range: 5.6 – 356 U/L) and 3-reagent (sample range: 12.7 – 324 U/L) methods. The samples were run in duplicates. The results generated correlation coefficients (r) of 0.99 and 0.98 for 1-reagent and 3-reagent methods, respectively. Deming regression analysis for 1-reagent and 3-reagent methods resulted in equations, $y = 0.99x + 1.54$ and $y = 0.98x + 0.73$, respectively. The sponsor's acceptance criterion for serum and plasma was $r \geq 0.9$.

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):*

4. Clinical cut-off:

Not Applicable.

5. Expected values/Reference range*:

The expected values of AST/GOT for Male (< 35 U/L at 37 °C) and Female (< 31 U/L at 37 °C) are based on the literature. The sponsor recommends in the labeling that each laboratory determine its own reference range for the population that it serves.

* IFCC 2002/6: IFCC Primary Reference Procedures for the Measurement of Catalytic Activity Concentrations of Enzymes at 37 °C, Part. 5. Reference Procedure for the Measurement of Catalytic Concentrations of Aspartate Aminotransferase, Clin.Chem.Lab.Med. 2002, 40(7): 725-733.

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.