

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

A. 510(k) Number:

k080485

B. Purpose for Submission:

New device

C. Measurand:

Aspartate Amino Transferase (AST/SGOT)

D. Type of Test:

Quantitative, enzymatic

E. Applicant:

DiaSys Diagnostic Systems GmbH

F. Proprietary and Established Names:

ASAT (GOT) FS assay

TruCal U calibrator (calibrator material for the ASAT FS assay)

TruLab N and TruLab P Controls (control material for the ASAT FS assay)

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
Aspartate amino transferase (AST/SGOT) Test System (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, Secondary (JIT)	Class II	21 CFR 862.1150, Calibrator	75 Clinical Chemistry (CH)
Product Code	Classification	Regulation Section	Panel
Single analyte control (JIX)	Class I	21 CFR 862.1660, Quality Control Material (assayed and unassayed)	75 Clinical Chemistry (CH)

H. Intended Use:

1. Intended use(s):

See Indication for use below.

2. Indication(s) for use:

ASAT (GOT) FS assay

The ASAT (GOT) FS assay is intended for quantitative *in vitro* diagnostic determination of the activity of the enzyme aspartate amino transferase (AST) in human serum and lithium heparin plasma on the Hitachi 917 instrument. Measurement of aspartate amino transferase levels aids in the diagnosis and treatment of certain types of liver and heart disease.

TruCal U

For *in vitro* diagnostic use on the Hitachi 917 instrument. TruCal U is used as a calibrator for the DiaSys ASAT (GOT) FS assay.

TruLab N and TruLab P Controls

For *in vitro* diagnostic use for quantitative testing on the Hitachi 917 instrument. TruLab N and TruLab P control sera are used to monitor accuracy and precision for the DiaSys ASAT (GOT) FS assay.

3. Special conditions for use statement(s):

For prescription use

4. Special instrument requirements:

Roche Hitachi 917 analyzer

I. Device Description:

The DiaSys aspartate amino transferase (AST) assay is supplied as ready-to-use, liquid reagents with two formats (with or without pyridoxal-5'-phosphate). The first format is a two reagents format without P-5-P, which consists of reagent A and reagent B. The second format is a three reagents format, which consists of reagent A, reagent B, and a third optional reagent, which is pyridoxal-5'-phosphate (P-5-P). For the two-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. Components included in the reagents are listed below:

1. Reagent A (Enzyme reagent) contains Tris buffer, pH 7.65 (110 mmol/L), L-Aspartate (320 mmol/L), lactate dehydrogenase (≥ 1200 U/L), and malate dehydrogenase (≥ 800 U/L).
2. Reagent B (substrate) contains 2-Oxoglutarate (65 mmol/L) and NADH (1 mmol/L).

3. Liquid pyridoxal-5'-phosphate contains Good's buffer, pH 9.6 (100 mmol/L) and pyridoxal-5'-phosphate (13 mmol/L).

The TruCal U calibrator is a lyophilized calibrator based on human serum and contains purified additives from human and animal origin, purified pharmaceuticals, and chemical additives. The AST added origins of porcine heart.

The TruLab N and TruLab P controls are lyophilized human-based control serum and contains purified human and animal components, purified drugs and non-organic components.

Human source materials was 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 names(s):

Roche AST assay, Roche calibrator for automated systems (C.f.a.s), and Roche Precinorm Universal Plus and Precipath Universal Plus controls

2. Predicate 510(k) number(s):

k924244, k990460, k042389

3. Comparison with predicate:

DiaSys ASAT FS assay:

Similarities and Differences		
Item	DiaSys AST assay (candidate device)	Roche AST assay (predicate device)
Intended Use	The AST/ GOT (IFCC) assay is intended for quantitative <i>in vitro</i> determination of the activity of the enzyme aspartate amino transferase (AST) in human serum and lithium heparin plasma on the Hitachi 917 instrument. Measurement of aspartate amino transferase levels aids in the diagnosis and treatment of certain types of liver and heart disease	In vitro test for the quantitative determination of aspartate amino transferase (AST) in human serum or plasma on Roche clinical chemistry analyzers
Assay protocol	1.) 2-reagent method: Modified IFCC reference method (without P-5-P) 2.) 3-reagent method: Original IFCC reference method (with P-5-P)	Same

Traceability	Standardized against the original IFCC formulation with and without pyridoxal phosphate	Same
Methodology	Enzymatic	Enzymatic
Analyzer	Roche Hitachi 917 analyzer	Roche auto chemistry analyzer
Calibrator	One level	Two levels: 1) A: Phosphate buffer 2) B: Gravimetrically prepared S-adenosyl-L-homocysteine (SAH) in phosphate buffer at defined concentrations.
Sample types	Serum or Heparin Plasma	Serum, EDTA or Heparin Plasma
Reportable range	7-700 U/L	4-800 U/L

TruCal U Calibrator:

Similarities and differences		
Item	Candidate Device	Predicate Device
Intended use	For <i>in vitro</i> diagnostic use on the Hitachi 917 instrument. TruCal U is used as a calibrator for the DiaSys ASAT (GOT) FS assay	For use in the calibration of the quantitative Roche methods on Roche clinical chemistry analyzers as specified in the value sheets
Form	Lyophilized human serum	Same
Levels	Single	Same

TruLab N and TruLab P Controls:

Similarities and differences		
Item	Candidate Device	Predicate Device
Intended use	For <i>in vitro</i> diagnostic use for quantitative testing on the Hitachi 917 instrument. TruLab N and TruLab P control sera are used to monitor accuracy and precision for the DiaSys ASAT (GOT) FS assay	For use in quality control by monitoring accuracy and precision for the quantitative methods as specified in the value sheets
Form	Lyophilized human serum	Same

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

CLSI Guideline, EP5-A2 *Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline Second edition (2004)*

CLSI Guideline, EP6-A *Evaluation of the Linearity of Quantitative Analytical Methods; Approved Guideline*

CLSI Guideline, EP7-A2 *Interference Testing in Clinical Chemistry; Approved Guideline-Second edition*

CLSI Guideline, EP9-A2 *Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline Second edition*

CLSI Guideline, EP17-A *Protocols for Demonstration, Verification, and Evaluation of Limits of Detection and Quantitation; Approved Guideline*

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.

Addition of pyridoxal-5-phosphate (P-5-P) stabilizes the transaminases and avoids falsely low values in samples containing insufficient endogenous P-5-P.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

A precision study was evaluated according to CLSI EP5-A guideline using three levels of serum samples. Samples were run twice per day in duplicate for 20 days on the Hitachi 917 analyzer (N=80). Precision data was calculated and summarized below:

Precision for method with P-5-P on the Hitachi 917 analyzer:

Levels	Mean (U/L)	Within run (%CV)	Between run (%CV)	Total precision (%CV)
Sample 1	42.0	1.08	2.42	2.84
Sample 2	83.2	1.12	3.26	4.41
Sample 3	541	0.93	0.14	1.22

Precision for method without P-5-P on the Hitachi 917 analyzer:

Levels	Mean (U/L)	Within run (%CV)	Between run (%CV)	Total precision (%CV)
Sample 1	29.7	1.32	3.19	3.81
Sample 2	74.0	1.13	3.95	5.06
Sample 3	560	0.83	0.57	1.30

b. Linearity/assay reportable range:

A linearity study was evaluated across the entire measuring range. A low serum sample and a high serum sample were mixed to prepare 11 different concentrations of AST and then diluted with saline (the recommended diluent). Each concentration was tested in quadruplicate and range tested was 0- 900 U/L for both methods (with P-5-P and without P-5-P) on the Hitachi 917 analyzer. Values were plotted for the expected concentrations (X) versus the observed concentrations (Y) and an appropriate line fitted by Passing Bablok method was calculated as follows:

With P-5-P: $y = 0.997x + 0.046$, $r = 0.9998$

Without-P-5-P: $y = 0.999x + 0.001$, $r = 0.9997$

The data provided supports the sponsor's claim that the assay has a reportable range of 7-700 U/L.

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

Traceability:

The DiaSys ASAT (GOT) FS assay is standardized against IFCC reference method. The two reagent format without P-5-P is traceable to the modified IFCC formulation while the three reagent format with P-5-P is traceable to the original IFCC formulation.

Value Assignment:

The concentration of the TruCal U calibrator, TruLab N and P controls are lot-specific and given in the value sheet of the corresponding lot. The value was determined using either the two reagent method without P-5-P or the three reagent method with P-5-P and by using the reagents specified by the method formats. Determinations of the value were performed under an internal protocol against a TruCal U master lot.

Stability of the TruCal U calibrator, TruLab N and P controls:

The shelf life and open vial stability testing protocols for the calibrators and controls and the acceptance criteria were described and found to be acceptable.

d. Detection limit:

A detection limit study was evaluated according to CLSI EP17-A guideline. The Limit of Blank (LoB) is defined as the highest value expected to see in a series of results on a sample that contains no analyte. The Limit of Detection (LoD) is the smallest amount that the method can reliably detect to determine presence or absence of an analyte. The Limit of Quantitation (LoQ) is the smallest amount the assay can reliably measure quantitatively and at which the uncertainty of the observed test result is less than or equal to the goal set (total error of a $CV \leq 20\%$). LoB was determined by running a blank sample 60 times on the Hitachi 917 analyzer. The limit of detection (LoD) and limit of quantitation (LoQ) were determined by running 4 low samples 60 times on the Hitachi 917. The detection limits are calculated as follows:

For method with P-5-P: LoB= 0.78 U/L, LoD=1.26 U/L, and LoQ=1.26 U/L

For method without P-5-P: LoB= 1.30 U/L, LoD=1.84 U/L, and LoQ=1.84 U/L

The reportable range for the assay is 7 – 700 U/L.

e. Analytical specificity:

An interference study was evaluated to determine the effect of common interference substances according to the CLSI EP7-A2 guideline. Two levels of human serum pools with different AST were tested. The following interference substances were tested: conjugated bilirubin, unconjugated bilirubin, hemoglobin, ascorbic acid and triglyceride. Stock solutions of the above chemicals were prepared and spiked into the tested samples with different concentrations. The % bias was calculated based on the differences between the spiked sample and the pool sample. The sponsor's acceptance criterion was <10% bias for the interferences to be considered as not significant. Results of the hemoglobin study demonstrated significant interference for hemoglobin; thus, the sponsor recommends that user not to use hemolyzed samples for this test and this information is provided in the labeling.

Results of the interference studies of various potential interferents were shown as follows:

For method without P-5-P:

Conjugated bilirubin: Interference $\leq 10\%$ for up to 60 mg/dL conj. bilirubin

Unconjugated bilirubin: Interference $\leq 10\%$ for up to 24 mg/dL unconj. bilirubin

Triglycerides: Interference $\leq 10\%$ for up to 400 mg/dL triglycerides

Ascorbic acid: Interference $\leq 10\%$ for up to 30 mg/dL ascorbic acid

For method with P-5-P:

Conjugated bilirubin: Interference $\leq 10\%$ for up to 36 mg/dL conj. bilirubin

Unconjugated bilirubin: Interference $\leq 10\%$ for up to 24 mg/dL unconj. bilirubin

Triglycerides: Interference $\leq 10\%$ for up to 400 mg/dL triglycerides

Ascorbic acid: Interference $\leq 10\%$ for up to 30 mg/dL ascorbic acid

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was performed using the DiaSys ASAT FS assay (candidate device) for both methods (with and without P-5-P) according to CLSI EP9-A2 guideline. Patient serum and lithium heparin plasma samples were used to evaluate against the Roche AST assay (predicate device). In order to cover the hard-to-find sample range some of the samples were spiked. All testing were performed using the Hitachi 917 analyzer. The method used to fit the linear regression line was Passing Bablok. A summary of the regression statistics is provided below:

Methods	N	Sample range	Slope	Intercept	R ²
Serum with P-5-P method	139	20-639	0.975	4.414	0.9999
Serum without P-5-P method	139	12-654	1.065	0.215	0.9994
Heparin plasma with P-5-P method	131	17-692	0.994	2.286	0.9998
Heparin plasma without P-5-P method	130	12-649	1.081	0.466	0.9998

b. Matrix comparison:

See method comparison study for both matrices in 2a. above

The sponsor recommends serum and lithium heparin plasma as samples to use.

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 ranges are provided in the labeling as follows: Male is < 35 U/L and Female is < 31 U/L for both with and without P-5-P methods (according to the literature that the sponsor cited)*

* 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.