510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K261364

B Applicant

Siemens Healthcare Diagnostics, Inc.

C Proprietary and Established Names

Atellica CH Acetaminophen 2 (ACTM)

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
LDP	Class II	21 CFR 862.3030 Acetaminophen Test System	Toxicology

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Measurand:

Acetaminophen

C Type of Test:

Quantitative enzymatic / colorimetric assay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Atellica CH Acetaminophen 2 (ACTM) assay is for in vitro diagnostic use in the quantitative determination of acetaminophen in human serum and plasma (K2 EDTA, lithium heparin, sodium heparin) using the Atellica CH Analyzer. Measurements obtained by this device are used in the diagnosis and treatment of acetaminophen overdose.

C Special Conditions for Use Statement(s):

Rx – For Prescription Use Only

D Special Instrument Requirements:

Atellica CH Analyzer

IV Device/System Characteristics:

A Device Description:

The assay consists of the following reagents:

Component	Active Ingredients	Volume
Reagent 1	Sodium periodate (1.88 mmol/L)	23.4 mL
Reagent 2	Arylacylamidase (>6,000 U/L); Ethyl-N-(3-sulfopropyl)m-anisidin (10 mmol/L)	13.5 mL

B Principle of Operation:

The Acetaminophen assay is an enzymatic assay based on the hydrolysis of acetaminophen by arylacylamidase to p-aminophenol and acetate. In the presence of ethyl-N-(3-sulfopropyl)-m-anisidin and a periodate catalyst, the p-aminophenol is converted to an indophenol derivate, and the reaction is measured colorimetrically at 694/545 nm. The increased absorbance at 694/545 nm is directly proportional to the concentration of acetaminophen in the sample.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Emit Tox Acetaminophen

B Predicate 510(k) Number(s):

K002974

C Comparison with Predicate(s):

Device & Predicate Device(s):	K261364 (Candidate)	K002974 (Predicate)

Device Trade Name	Atellica CH Acetaminophen 2 (ACTM)	Emit Tox Acetaminophen
General Device Characteristic Similarities		
Intended Use/Indications For Use	For in vitro diagnostic use in the quantitative determination of acetaminophen in human serum and plasma. Measurements obtained by this device are used in the diagnosis and treatment of acetaminophen overdose.	Same
General Device Characteristic Differences		
Measurement Range	2.0 – 200 µg/mL	0.25 – 200 µg/mL
Methodology	Enzymatic (arylacylamidase) coupled with colorimetric measurement at 694/545 nm	Enzyme immunoassay coupled with spectrophotometric measurement at 340 nm.
Sample Type	Serum and Plasma (K2 EDTA lithium heparin, sodium heparin)	Serum and Plasma (EDTA, heparin, citrate and oxalate/fluoride)

VI Standards/Guidance Documents Referenced:

- CLSI EP17-A2 2nd Edition: *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures*, FDA Recognition Number: 7-233
- CLSI EP05-A3: *Evaluation of Precision Performance of Quantitative Measurement Methods,* FDA Recognition Number: 7-251
- ISO 17511 2nd Edition: *In vitro diagnostic medical devices - Requirements for establishing metrological traceability of values assigned to calibrators, trueness control materials and human samples*, FDA Recognition Number: 7-305
- CLSI EP09c 3rd Edition: *Measurement Procedure Comparison and Bias Estimation Using Patient Samples,* FDA Recognition Number: 7-296
- CLSI EP06 2nd Edition: *Evaluation of the Linearity of Quantitative Measurement Procedures,* FDA Recognition Number: 7-306
- CLSI EP07 3rd Edition: *Interference Testing in Clinical Chemistry*, FDA Recognition Number: 7-275

- CLSI EP34 1st Edition: *Establishing and Verifying an Extended Measuring Interval Through Specimen Dilution and Spiking,* FDA Recognition Number: 7-290
- CLSI EP25 2nd Edition: *Evaluation of Stability of In Vitro Medical Laboratory Test Reagents* FDA Recognition Number: 7-318 I

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Precision studies were performed using one pooled serum samples and three individual unique serum samples each spiked with acetaminophen. Samples were assayed in duplicate (2), with two runs per day for 20 days on one reagent lot and one Atellica CH Analyzer for analyses of repeatability, between-run, between-day and within-lab precision. Between-lot, between-instrument precision and reproducibility were also assessed by testing replicates of five (5), one run per day, for five days using three reagent lots on three Atellica CH analyzers. Summary of precision results are shown below.

Serum Sample	N	Mean (µg/mL)	Repeatability		Between-Run		Between-Day		Within-Lab	
			SD (µg/mL)	CV (%)	SD (µg/mL)	CV (%)	SD (µg/mL)	CV (%)	SD (µg/mL)	CV (%)
1	80	4.7	0.07	1.5	0.07	1.5	0.11	2.3	0.15	3.2
2	80	45.3	0.18	0.4	0.19	0.4	0.67	1.5	0.71	1.6
3	80	165.1	0.48	0.3	0.5	0.3	2.26	1.4	2.37	1.4
4	80	98.1	0.29	0.3	0.38	0.4	1.33	1.4	1.42	1.4

Serum Sample	N	Mean (µg/mL)	Between-Lot		Between-Instrument		Reproducibility	
			SD (µg/mL)	CV (%)	SD (µg/mL)	CV (%)	SD (µg/mL)	CV (%)
1	225	4.6	0.06	1.3	0.11	2.4	0.2	4.3
2	225	44.4	0.13	0.3	0.29	0.7	0.41	0.9
3	225	162.3	0.55	0.3	1.06	0.7	1.37	0.8
4	225	96.4	0.17	0.2	0.59	0.6	0.85	0.9

2. Linearity:

Linearity for the Atellica CH Acetaminophen 2 ACTM assay was assessed following CLSI EP06 2nd ED: Evaluation of Linearity of Quantitative Measurement Procedures. A dilution series of nine (9) levels was prepared by mixing a high serum specimen that was spiked with acetaminophen and a blank serum specimen not containing the analyte. Each resulting acetaminophen level (1.7, 6.0, 10.0, 30.0, 60.0, 90.0, 120.0, 150.0, and 210.0 µg/mL) was assayed in replicates of four using one reagent lot, on one Atellica CH analyzer.

The maximum deviation within the reportable range was -1.8 µg/mL or 3.0%. The results of the linearity studies support the sponsor's claimed measuring interval of 2.0 – 200 µg/mL.

Auto Dilution Validation

Dilution accuracy was evaluated following CLSI EP34 to extend the measurement range to 600 µg/mL. Acetaminophen concentrations between 262.0 to 543.6 µg/mL were prepared by spiking five serum specimens with known acetaminophen. The acetaminophen concentration of each sample was assigned by assaying on the predicate device. Each sample was automatically diluted at a 1:3 dilution and run in replicates of 5 using one reagent lot on two instruments. The % recovery were all within ± 7% of the expected value.

3. Analytical Specificity/Interference:

Interference studies were performed as described in CLSI EP07 3rd ED: Interference Testing in Clinical Chemistry and CLSI EP37 1st ED: Supplemental Tables for Interference Testing in Clinical Chemistry.

Matched test control samples were prepared for each potential interferent by spiking native human serum containing acetaminophen concentrations at approximately 7.5 – 12.5 µg/mL and 22.5 – 37.5 µg/mL and tested in replicates of five. The highest interferent concentration tested that results in interference ≤10% or within ±2 µg/mL is determined as the concentration with no significant interference.

Endogenous Interference

Potential Endogenous Interferent	**Highest Tested Interferent Concentration with no significant interference (mg/dL)**
Bilirubin – conjugated	60
Bilirubin – unconjugated	30
Hemoglobin	500
Lipemia (Intralipid)	500
Lipemia (from human triglyceride fraction)	1500
Total Protein	10 g/dL

Exogenous Interference

Interferent	**Highest Tested Interferent Concentration with no significant interference**

Acetylsalicylic Acid	117.3 mg/dL
Amitriptyline	0.1 mg/dL
Ampicillin	33.3 mg/dL
Benzocaine	560 mg/L
Cefoxitin	69 mg/dL
Codeine	0.141 mg/dL
Cyclosporine	1.2 mg/dL
Cysteamine	220 µmol/L
Dapsone	5.9 mg/L
Dipyrone/Metamizole	10 mg/dL
2,5-Dihydroxybenzoic acid	117 µmol/L
Doxycycline	4.5 mg/dL
Ibuprofen	50 mg/dL
Imipramine	0.0315 mg/dL
L-Ascorbic Acid	324 mg/dL
L-Cysteine	1 mg/mL
Levodopa	0.75 mg/dL
L-Methionine	500 µg/mL
Methyldopa	2.25 mg/dL
Metoclopramide	0.225 mg/dL
Metronidazole	12.3 mg/dL
N-Acetylcysteine	100 mg/dL
N-Acetylprocainamide	4.8 mg/dL
NAPQI (N-Acetyl-4-benzoquinoneimine)	0.375 mg/dL
p-Aminosalicylic acid	81.2 mg/dL
Phenylbutazone	89.1 mg/dL
Procainamide	4.8 mg/dL
Rifampicin	7.5 mg/dL
Salicylic acid	60.8 mg/dL
Tetracycline	2.4 mg/dL
Theophylline	6 mg/dL

4. Detection Limit and Assay Reportable Range:

The Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ) were determined in accordance with CLSI EP17-A2.

The LoB and LoD were each determined using four samples (blank samples and low-level samples, respectively) assayed in five replicates per day over three days, across three reagent lots, yielding 60 total measurements per reagent lot.

The LoB for each reagent lot was calculated nonparametrically as the value at the 95th percentile of the ranked blank sample measurement results. The overall assay LoB was defined as the maximum LoB observed across all three reagent lots.

The LoD for each reagent lot was calculated parametrically using the following equation: **LoD = LoB + c*p* × *SD*L** where *cp* is the correction factor derived from the 95th percentile of the standard normal (Gaussian) distribution, and *SD*L is the pooled standard deviation of measurement results across all low-level samples. The overall assay LoD was defined as the maximum LoD observed across all three reagent lots.

The LoQ was determined using five samples assayed in replicates of eight over five days on three reagent lots yielding a total of 40 measurements per sample per reagent lot. LoQ for each reagent lot was defined as the lowest analyte concentration at which the within-laboratory coefficient of variation (CV) was ≤ 15% or the LoD, whichever was greater. The largest LoQ calculated among the lots was the overall assay LoQ.

LoB	0.1 µg/mL
LoD	0.5 µg/mL
LoQ	2.0 µg/mL

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

The Atellica CH Acetaminophen ACTM calibrator is traceable to an internal standard manufactured using United State Pharmacopeia reference standard. Traceability was established following ISO 17511:2020.

Studies support the following claims:

	Claim
Pack Calibration	3 days
Lot Calibration	30 days
On-board Stability	15 days

6. Assay Cut-Off:

Not applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:

A method Comparison study was performed in accordance with CLSI EP09c-ED3. A total of 104 native human serum patient samples ranging from 2.1 – 181.6 µg/mL were tested using the candidate device on the Atellica CH analyzer and the predicate device.

Deming regression analysis resulted in a slope of 1.00 µg/mL, y-intercept of 0.10 µg/mL and a correlation coefficient of 0.998.

2. Matrix Comparison:

A matrix comparison study was conducted for serum, lithium heparin plasma, sodium heparin plasma, and K2 EDTA plasma. Matched samples set from the same donor were drawn into four different tube types: serum, lithium heparin plasma, sodium heparin plasma, and K2 EDTA plasma. A total of 51 samples were assayed using one reagent lot over seven days. Specimen equivalence was evaluated by Deming regression analysis comparing serum to lithium heparin plasma, sodium heparin plasma, and K2 EDTA plasma.

Comparative Specimen Type (X)	Candidate Specimen Type (Y)	Sample Range (µg/mL)	N	Regression Equation (µg/mL)	r
Serum	Lithium Heparin Plasma	3.7 - 184.7	51	Y = 1.01X - 0.1	1.00
	Sodium Heparin Plasma	3.7 - 184.7	51	Y = 1.00X - 0.1	1.00
	K2 EDTA Plasma	3.7 - 184.7	51	Y = 1.01X - 0.5	1.00

C Clinical Studies:

1. Clinical Sensitivity:

   Not applicable

2. Clinical Specificity:

   Not applicable

3. Clinical Cut-Off:

   Not applicable

4. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

   Not applicable

D Expected Values/Reference Range:

Expected values were cited from Rifai, Nader, Horvath Andrea Rita, Wittwer Carl T. *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics*. 6th ed. Elsevier; 2018:1801.

Expected Values/Reference Range	Concentrations (µg/mL)
Therapeutic Range	10 - 30
Toxic Concentration 4 hours post-ingestion	>200
Toxic Concentration 12 hours post-ingestion	>50

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.