Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
www.fda.gov

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

## I Background Information:

### A 510(k) Number

K191454

### B Applicant

Siemens Healthcare Diagnostics Inc.

### C Proprietary and Established Names

Atellica® CH Amylase_2 (AMY_2)

### D Regulatory Information

| Product Code(s) | Classification | Regulation Section | Panel |
|---|---|---|---|
| JFJ | Class II | 21 CFR 862.1070 - Amylase Test System | CH - Clinical Chemistry |

## II Submission/Device Overview:

### A Purpose for Submission:

New device

### B Measurand:

Amylase

### 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 Amylase_2 (AMY_2) assay is for in vitro diagnostic use in the quantitative determination of amylase activity in human serum, plasma (lithium heparin), and urine using the Atellica® CH Analyzer. Such measurements are used primarily in the diagnosis and monitoring of acute pancreatitis (inflammation of the pancreas).

### 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:

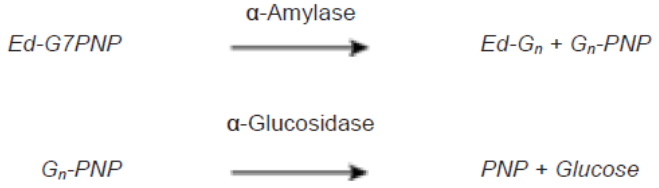
The Atellica® CH Amylase_2 (AMY_2) reagents are packaged in 2 packs with 2 wells per pack. The wells have a divider which keeps the two liquid chambers separate.

Each well of Pack 1 (P1) contains 18.7 mL of Reagent 1 (R1) which consists of:
α-Glucosidase (≥ 4 kU/L); sodium azide (0.09%)

Each well of Pack 2 (P2) contains 6.5 mL of Reagent 2 (R2) which consists of:
Ethylidene-4-NP-G7 (22 mmol/L), sodium azide (0.09%)

### B Principle of Operation:

The Atellica® CH AMY_2 assay uses ethylidene blocked *p*-nitrophenyl-maltoheptaoside as substrate. The indicator enzyme α-glucosidase, used to release *p*-nitrophenol (PNP), is also employed in the assay. The terminal glucose of the substrate is chemically blocked, preventing cleavage by the indicator enzymes. The released *p*-nitrophenol is measured at 410/694 nm.



**C Instrument Description Information:**

| Modes of Operation | Yes | No |
|---|---|---|
| Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device? | ☐ | ☒ |
| Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission? | ☐ | ☒ |
| **Software** | | |
| FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types. | ☐ | ☒ |

1. Instrument Name:

   Atellica® CH Analyzer

2. Specimen Identification:

   Manual entry or barcode identification.

3. Specimen Sampling and Handling:

   Samples are identified and delivered by the sample handler (Direct Load), which is part of the Trinidad CH system.

4. Calibration:

   62 days for a reagent lot; 31 days for an individual pack well

5. Quality Control:

   Use at least two levels (low and high) of the appropriate quality control material of known analyte concentration, referring to the lot-specific value sheet provided.

**V Substantial Equivalence Information:**

**A Predicate Device Name(s):**
Roche Cobas Ready Amylase Reagent

**B Predicate 510(k) Number(s):**
K903309

**C Comparison with Predicate(s):**

| **Device & Predicate Device(s):** | K191454 | K903309 |
|---|---|---|
| Device Trade Name | **Atellica® CH Amylase_2 (AMY_2)** | **Roche Cobas Amylase Reagent** |
| **General Device Characteristic Similarities** | | |
| Intended Use/Indications For Use | For *in vitro* diagnostic use in the quantitative determination of amylase activity in human serum, plasma, and urine. Such measurements are used primarily in the diagnosis and monitoring of acute pancreatitis (inflammation of the pancreas). | Same |
| Measurand | Amylase | Same |
| Device Technology | Enzymatic colorimetric assay | Same |
| Sample Type | Serum, Lithium Heparin Plasma, and Urine | Same |
| **General Device Characteristic Differences** | | |
| Measuring Interval | 20 to 1500 U/L | 3 to 1500 U/L |
| Expected Values | Serum/Li-Heparin Plasma: 30-118 U/L<br>Urine: ≤ 650 U/L | Serum/Li-Heparin Plasma:<br>Men/Women: 28-200 U/L<br>Spontaneously Voided Urine:<br>Men: 16-491 U/L<br>Women: 21-447 U/L |
| Tracebility | Traceable to IRMM/IFCC-456 Pancreatic α-Amylase Reference Material. | This method has been standardized against a Roche system reagent. |
| Calibration Frequency | 62 days for a reagent lot; 31 days for an individual pack well | After reagent lot change; as required following QC procedures |

## VI Standards/Guidance Documents Referenced:

CLSI EP07-A2, Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition.

CLSI EP05-A3, Evaluation of Precision Performance of Quantitative Measurement Methods: Approved Guideline – Third Edition.

CLSI EP06-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline.

CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures – Second Edition.

CLSI EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline.

CLSI EP28-A3, Defining, Establishing, And Verifying Reference Intervals In The Clinical Laboratory; Approved Guideline – Third Edition.

## VII Performance Characteristics (if/when applicable):

### A Analytical Performance:

1. Precision/Reproducibility:

Precision studies were performed according to the *CLSI EP05-A3 Evaluation of Precision Performance of Quantitative Measurement Methods* guideline. Precision was assessed by testing each sample using two replicates, two times per day, for at least 20 days for a total of at least 80 replicates. The samples tested were commercial controls (for both serum and urine), spiked pools (for serum, urine, and plasma), and a diluted urine pool. The results of precision studies are summarized below.

| Sample Type | n | Mean U/L | Repeatability | | Within-Lab Precision | |
|---|---|---|---|---|---|---|
| | | | SD U/L | CV (%) | SD U/L | CV (%) |
| Sample 1 | 80 | 52 | 0.6 | 1.1 | 0.7 | 1.4 |
| Serum QC | 80 | 187 | 0.8 | 0.4 | 1.1 | 0.6 |
| Sample 2 | 80 | 1128 | 2.2 | 0.2 | 4.3 | 0.4 |
| Urine QC | 80 | 58 | 1.0 | 1.7 | 1.3 | 2.2 |
| Urine 1 | 80 | 183 | 0.8 | 0.4 | 2.3 | 1.3 |
| Urine 2 | 80 | 1260 | 9.3 | 0.7 | 21.5 | 1.7 |

2. Linearity:

A linearity study was conducted based on the *CLSI EP6-A Evaluation of the Linearity of Quantitative Measurement Procedures* guideline.

Nine serial dilutions were (13 U/L to 1622 U/L for serum, 12 U/L to 1720 U/L for urine) were prepared by mixing high and low concentrations samples across the measurement interval. Five replicates were measured for each sample, with the mean used for the calculations.

The mean results (y-axis) were plotted against the expected results (x-axis). The results of the linear regression analysis are as follows:

Serum (unweighted linear regression): $y = 0.99826x - 3.13$, $R^2 = 1.000$
Urine (weighted linear regression): $y = 0.9673x - 7.10$, $R^2 = 0.999$

The results of the study support the sponsor's claim that the Atellica® CH Amylase_2 (AMY_2) assay is linear across the measuring range of 20 to 1500 U/L for serum and urine specimens.

The sponsor also conducted an auto-dilution recovery study to evaluate the auto-dilute feature available for both serum and urine matrices. Using CH diluent, 3-fold manual dilutions of serum and urine pools were made. The study protocol and acceptance criteria were reviewed and found to be acceptable. Results of this study supported the sponsor's claim that samples with amylase concentrations above 1500 U/L can be diluted onboard the analyzer to obtain results up to 4500 U/L for serum and urine.

3. Analytical Specificity/Interference:

Interference studies were performed in accordance with the *CLSI EP07-A2 Interference Testing in Clinical Chemistry* guideline. Studies were conducted using a "paired difference worst-case scenario" approach in which the compounds were spiked into fresh sample pools (serum and urine) containing either high (400 U/L) or low (100 U/L) levels of measurand. Test and control samples for each measurand level were tested in five replicates. The sponsor define interference as >10% difference between the test and control samples.

The results of interference studies are summarized below.

| Substance | Substance Test Concentration (mg/dL) |
|---|---|
| Hemoglobin | 500 |
| Bilirubin, conjugated | 30 |
| Bilirubin, unconjugated | 30 |
| Intralipid® | 650 |

Exogenous interferences:

| Substance | Substance Test Concentration (mg/dL) |
|---|---|
| Acetaminophen | 30 |
| Acetylsalicylic Acid | 200 |
| Ascorbic Acid | 20 |

4. Assay Reportable Range:

   The assay has a reportable range of 20 to 1500 U/L for serum, plasma, and urine specimens.

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

   The Atellica® CH AMY_2 (AMY_2) assay is traceable to the IRMM/IFCC-456 Pancreatic Alpha-Amylase Reference Material.

6. Detection Limit:

   The Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ) were evaluated in accordance with *CLSI EP17-A2 Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures*.

   LoB
   Four samples with no analyte were tested in replicates of 20 for 3 days, with one run per day, and using three reagent lots. LoB was determined using a nonparametric approach (LoB Rank Position = 0.5 + 0.95 × B, where B = total reps = 240; rank = 228.5.)

   LoD
   Four low analyte samples were tested in replicates of 20 for 3 days, with one run per day, using 3 reagent lots. LoD was determined using a nonparametric approach and corresponded to the lowest concentration of amylase that can be detected with a probability of 95%.

   LoQ
   Four low analyte samples were processed in replicates of 10 on 3 reagent lots for 3 days on one instrument for a total of 120 measurements per lot. The LoQ was defined as the concentration that met a Total Error (TE) goal of ≤30%. TE was calculated as TE = |bias| + 2 × SD.

   The results of the detection limit studies are presented in the table below:

| Matrix | LoB | LoD | LoQ | Claimed Range |
|---|---|---|---|---|
| Serum | 1 U/L | 7 U/L | 18 U/L | 20-1500 U/L |
| Urine | 1/U/L | 9 U/L | 19 U/L | 20-1500 U/L |

7. Assay Cut-Off:

   Not applicable.

8. Accuracy (Instrument):

   Not applicable.

9. Carry-Over:

   Not applicable.

## B Comparison Studies:

1. Method Comparison with Predicate Device:

   A method comparison study was conducted by testing remnant de-identified serum and urine samples, including native and spiked samples (less than 10%). For the serum method comparison, one replicate was processed on the predicate device, and two were processed on the candidate device. For the urine method comparison, two replicates were processed on each. Only the first replicate results were used in the data analysis. Results were analyzed using weighted Deming regression.

   Results of regression analysis are summarized below.

| Specimen Type | N | Slope | Intercept | r | Test range U/L (per Roche cobas) | Claimed Measuring Range U/L |
|---|---|---|---|---|---|---|
| Serum | 118 | 1.09 | 0 | 0.996 | 28-1294 | 20-1500 |
| Urine | 114 | 1.11 | -1 | 0.998 | 20-1194 | 20-1500 |

2. Matrix Comparison:

   Matched serum and lithium heparin plasma sets were processed with two replicates, using only the first replicate for analysis. Sixty-six (66) matched serum/plasma samples that ranged from 36 U/L (serum) to 1419 U/L (serum) were assayed in duplicate. The study set included 66 samples with concentrations ranging from 36 U/L to 1419 U/L. The results were compared using Deming linear regression statistics. The results are as follows:

   $y = 1.00 x + 0,\ r = 1.000$

   The results of the study support the sponsor claims that the Atellica® CH Amylase_2 (AMY_2) can be used with serum and lithium heparin plasma samples.

## C Clinical Studies:

1. Clinical Sensitivity:

   Not applicable.

2. Clinical Specificity:

   Not applicable.

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

   Not applicable.

## D Clinical Cut-Off:

Not applicable.

## E Expected Values/Reference Range:

Reference interval studies were conducted according to *CLSI EP28-A3 Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory* to verify serum and urine values cited from the literature. A total of 20 serum specimens and urine specimens obtained for healthy adults were tested. Results of the verification study support the serum and urine reference ranges which were established through literature.

| Specimen Type | Reference Interval |
|---|---|
| Serum/plasma[1] | 30-118 U/L |
| Urine[2] | ≤ 650 U/L |

[1] Thornton W, Levine R, Levine JB. *Evidence-Based Medicine and Test Utilization: Developing Reference Intervals for Clinical Chemistry Systems Using the CLSI C28-A2 Guideline*. White Paper on file at Siemens Medical Solutions Diagnostics; 2007:11. Provided per LR email request 7/1/2019.

[2] Wu AHB. *Tietz Clinical Guide to Laboratory Tests*. 4th Ed. St. Louis, MO: WB Saunders Co.; 2006:104.

# 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.