July 30, 2019

Siemens Healthcare Diagnostics Inc.
Catherine Daigle
Regulatory Technical Specialist
500 GBC Drive
P.O. Box 6101, M/S 514
Newark, DE 19714

Re: K191454
Trade/Device Name: Atellica® CH Amylase_2 (AMY_2)
Regulation Number: 21 CFR 862.1070
Regulation Name: Amylase Test System
Regulatory Class: Class II
Product Code: JFJ
Dated: May 30, 2019
Received: May 31, 2019

Dear Catherine Daigle:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Kellie B. Kelm, Ph.D.
Acting Director
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
k191454

Device Name
Atellica® CH Amylase_2 (AMY_2)

Indications for Use *(Describe)*

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).

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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Siemens Healthcare Diagnostics Inc.
500 GBC Drive, Mailstop 514
P.O. Box 6101
Newark, DE 19714-6101

510(k) Summary for Atellica® CH Amylase_2 (AMY_2)

This summary of 510(k) safety and effectiveness information is submitted in accordance with the requirements of SMDA 1990 and 21 CFR §807.92.

ASSIGNED 510(K) NUMBER

The assigned 510(k) number is: _k191454_____.

APPLICANT AND DATE

Catherine I. Daigle, MS
Siemens Healthcare Diagnostics Inc.
500 GBC Drive, M/S 514
Newark, DE 19714-6101
Email: catherine.i.daigle@siemens-healthineers.com
Phone: 302-631-7310
Fax: 302-631-6299

May 30, 2019

MANUFACTURER

Siemens Healthcare Diagnostics Inc.
511 Benedict Ave
Tarrytown, NY 10591
Registration Number: 2432235

REGULATORY INFORMATION

Regulatory Submission for the Atellica® CH Amylase_2 (AMY_2)

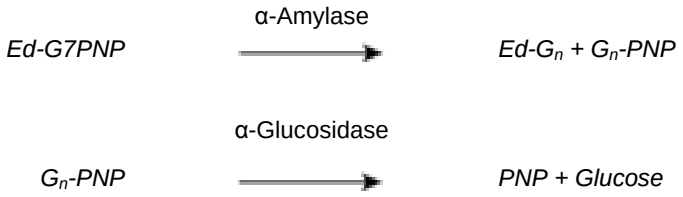
Common Name:	Photometric Method, Amylase
Proprietary Name:	Atellica CH Amylase_2 (AMY_2)
Classification Name:	Amylase Test System
Regulation Number:	21CFR862.1070
Classification:	Class II
Product Code:	JFJ
Panel:	Clinical Chemistry
Predicate Device:	Roche Cobas Amylase Reagent (k903309)

DEVICE DESCRIPTION

ATELLICA CH AMYLASE_2 (AMY-2)

The Atellica® CH Amylase_2 (AMY_2) assay is based on the procedure of Jensen and Wydeveld.[1] 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.

Reaction Equation



Serum, lithium heparin plasma and urine specimens may be used. The reagent is stored unopened at 2 – 8 °C and is stable for use on system for 31 days. Calibration is performed every 62 days for a reagent lot or every 31 days for an individual pack well.

1. Jenson AP, Wydeveld A. α-(p-nitrophenyl) maltohexaside as a substrate for the assay of amylase. *Nature.* 1958; 182:525-526.

INTENDED USE / INDICATIONS FOR USE

ATELLICA CH AMYLASE 2 (AMY-2)

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).

COMPARISON OF TECHNOLOGICAL CHARACTERISTICS

Below is a features comparison for the Atellica® CH Amylase_2 (AMY_2) assay and the predicate device:

Feature	**Predicate Device:** Roche Cobas Amylase Reagent (k903309)	**New Device:** Atellica® CH Amylase_2 (AMY_2)
Intended Use :	*In vitro* test for the quantitative determination of α-amylase in human serum, plasma and urine on Roche/Hitachi **cobas c** systems.	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).
Device Technology:	Enzymatic colorimetric assay	Same
Sample Type:	Serum, Li-Heparin Plasma and Urine	Same
Expected Values:	Serum/Li-Heparin Plasma: Men/Women: 28-100 U/L Spontaneously Voided Urine: Men: 16-491 U/L Women: 21-447 U/L	Serum/Li-Heparin Plasma: 30-118 U/L Urine : ≤ 650 U/L

Feature	**Predicate Device:** Roche Cobas Amylase Reagent (k903309)	**New Device:** Atellica® CH Amylase_2 (AMY_2)
Standardization:	This method has been standardized against Roche system reagent using calibrated pipettes together with a manual photometer providing absolute values and substrate-specific absorptivity, ε.	Traceable to IRMM/IFCC-456 Pancreatic Alpha-Amylase Reference Material and commutable to the IFCC Alpha-Amylase Primary Reference Procedure as established by patient sample correlation.
Calibration Frequency:	• After reagent lot change • As required following quality control procedures	62 days for a reagent lot; 31 days for an individual pack well
Analytical Measuring Interval:	Serum/Plasma/Urine: 3-1500 U/L	Serum/Plasma/Urine: 20-1500 U/L
Interferences:	No significant interference for: Bilirubin (Conjugated) at a concentration of: 60 mg/dL Bilirubin (Unconjugated) at a concentration of: 60 mg/dL Lipemia (Intralipid®) at a concentration of: 1500 mg/dL Hemoglobin at a concentration of: 500 mg/dL	No significant interference for: Bilirubin (Conjugated) at a concentration of: 30 mg/dL Bilirubin (Unconjugated) at a concentration of: 30 mg/dL Lipemia (Intralipid®) at a concentration of: 650 mg/dL Hemoglobin at a concentration of: 500 mg/dL

SUMMARY OF PERFORMANCE TESTING

Assay performance comparison results for the Atellica® CH Amylase_2 (AMY_2) were obtained by processing the appropriate body fluids. Summary statistics for each are provided. These data demonstrate substantial equivalency of the Atellica® CH Amylase_2 (AMY_2) compared to the predicate device. The following data represent typical assay performance.

DETECTION LIMIT

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

Assessment of LoB was the 95th percentile of all values (sorted from lowest to highest), using non-parametric approach.

LoB Rank Position = 0.5 +0.95*B, where B=total reps=240; Rank = 228.5

Atellica® CH Amylase_2 (AMY_2) – Detection Capability		
Limit	Protocol	Result
LoB	4 samples with no analyte were tested (N=20) for 3 days, one run per day, 3 reagent lots	1 U/L Serum/Plasma/Urine
LoD	4 low analyte samples were tested (N=20) for 3 days, one run per day, 3 reagent lots	7 U/L Serum/Plasma 9 U/L Urine

LOQ

The Limit of Quantitation (LoQ) for serum/plasma and urine was determined as described in *CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures*. Total Error is calculated using: TE = |bias| + 2 * SD.

For both serum/plasma and urine fluids, 4 low samples were processed on three reagent lots for three days, on one instrument for a total of 120 measurements per lot. For serum/plasma, the measured LoQ was 18 U/L in support of the low end of the measuring interval of 20 U/L for serum and plasma samples. For urine, the measured LoQ was 19 U/L in support of the low end of the measuring interval of 20 U/L for urine samples. The LoQ claim of 20 U/L for serum/plasma and urine are each based on a total of 120 determinations with a total error goal of ≤ 30% for serum/plasma specimens and ≤ 30% for urine specimens.

LINEARITY

Linearity was evaluated with 9 samples which spanned the assay measuring interval for serum specimens and 9 samples which spanned the assay measuring interval for urine specimens. Each was prepared by mixing high and low concentration samples across the measurement interval as described in *CLSI EP06-A, Evaluation of the Linearity of Quantitative Measurement Procedures*. The high sample was prepared by spiking

native serum or urine pools with amylase. Low pools were created by diluting serum and urine samples with CH diluent. Five replicates were measured for each sample. The mean of these replicates was used for the calculations.

The assay was considered linear across the measuring interval if the p-values of nonlinear terms in the quadratic and cubic fit equations are nonsignificant ($p > 0.05$). If any of the aforementioned p-values are ≤ 0.05, then linearity was determined via an allowable bias of ≤ 10% or ≤ 10 U/L, whichever is greater, for the observed values vs. the linear fit. Linearity of the Atellica CH Amylase_2 (AMY_2) was demonstrated with both serum and urine specimens to encompass the measuring interval of 20 to 1500 U/L for serum, plasma, and urine specimens.

PRECISION

Precision testing was performed in accordance with *CLSI EP05-A3, Evaluation of Precision Performance of Quantitative Measurement Methods*. Precision was tested using n = 2 replicates, two times per day for at least 20 days for a total of 80 replicates per sample with controls, serum, plasma, and urine pools on one instrument. Analysis of variance (ANOVA) was used to evaluate the data consistent with the recommendations of EP05-A3. The data are summarized in the following table.

			Repeatability		Within-Lab Precision	
Sample Type	**n**	**Mean U/L**	**SD[a] U/L**	**CV[b] (%)**	**SD[a] U/L**	**CV[b] (%)**
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

[a] SD = standard deviation

[b] CV = coefficient of variation

INTERFERENCES

CLSI EP07-A2, Interference Testing in Clinical Chemistry, was followed for the interference testing. The interference study was conducted using a "paired difference worst case scenario" approach where these compounds were spiked into fresh sample pools containing either low or high levels of measurand in serum and urine pools.

Bias is the difference in the results between the control sample (without the interferent) and the test sample (contains the interferent) expressed in percent. Bias exceeding 10% is considered interference. Dilution studies were conducted to determine the level at which the spiked substance no longer displayed significant interference. Dilution studies were conducted at two analyte concentrations, if both sample pools show significant interference. This study was conducted as needed for both serum pools.

Approximate Concentration (within 15%) of Analytes in Test Pools			
Analyte	Matrix	Low	High
Amylase	Serum	100 U/L	400 U/L
Amylase	Urine	100 U/L	400 U/L

No interference was detected a the following analyte concentrations.

Interference Testing for Serum and Urine

Substance	Substance Test Concentration Common Unit
Hemoglobin	500 mg/dL
Bilirubin, conjugated	30 mg/dL
Bilirubin, unconjugated	30 mg/dL
Lipemia (Intralipid®)	650 mg/dL
Acetaminophen	30 mg/dL
Ascorbic Acid	20 mg/dL
Acetylsalicylic Acid	200 mg/dL

METHOD COMPARISON

The predicate device selected for the method comparison study was the Roche Cobas Amylase (AMYL2) Reagent. Remnant de-identified samples were tested. No patient history information was obtained on these samples. Inclusion/exclusion data criteria are not applicable. The study included native and spiked samples to properly span the assay measuring interval.

These studies were conducted internally by Siemens Healthcare Diagnostic Inc. R&D organization personnel, and externally by a contracted laboratory. The personnel conducting the study were laboratory technicians with training similar to personnel who would conduct the tests in a hospital laboratory setting. They were trained on the operation of both the device and the predicate device. A split sample method comparison, following *CLSI EP09-A3, Measurement Procedure Comparision and Bias Estimation Using Patient Samples*, demonstrated good agreement between the Atellica® CH Amylase_2 (AMY_2) and the predicate Roche Cobas Amylase (AMYL2) assay with patient samples.

The results across the full assay intervals were analyzed using weighted Deming regression. For the serum method comparison, one replicate was processed on the Cobas while two replicates were processed on the Atellica. For the urine method comparison two replicates were processed for each sample on both systems. Only the first replicate results were used in statistical analysis. Indicated samples were spiked with pancreatic amylase to span the assay measuring interval.

Specimen Type	Comparison Assay (x)	N	r	Regression Equation	Sample Range (on the Roche Cobas)
Serum	Roche Cobas AMYL2	118	0.996	y = 1.09x + 0 U/L	28-1294 U/L
Urine	Roche Cobas AMYL2	114	0.998	y = 1.11x – 1 U/L	20-1194 U/L

MATRIX EQUIVALENCY

Matched serum and lithium heparin plasma sets were processed with N= 2 replicates using only the first replicate for analysis on the Atellica® CH Amylase_2 (AMY_2) assay. Some samples were spiked with amylase to obtain samples spanning the assay measuring interval. The table below summarizes the Deming linear regression statistics.

Specimen Type	Comparison Assay (x)	N	r	Regression Equation	Sample Range
Plasma (Lithium heparin)	Atellica® CH AMY_2 serum	66	1.000	y = 1.00x + 0 U/L	36 -1419 U/L

EXPECTED VALUES

Reference intervals for healthy adults were verified on the Atellica® CH Analyzer in accordance with *CLSI EP28-A3, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory*. As with all *in vitro* diagnostic assays, each laboratory should determine its own reference interval for the diagnostic evaluation of patient results. Consider these values as guidance only.

Group	Specimen type	Reference Interval common unit (SI unit)
Adults	Serum/plasma[1]	30 to 118 U/L
Adults	Urine[2]	≤ 650 U/L

2. Data on file at Siemens Healthcare Diagnostics. (Evidence-based Medicine and Test Utilization Developing Reference Intervals for Clinical Chemistry Systems Using the CLSI C28-A2 Guideline)
3. Wu AHB. Tietz Clinical Guide to Laboratory Tests. 4th ed. Philadelphia, PA: WB Saunders Co; 2006:104.

Extended Measuring Interval

The Atellica® CH Amylase_2 assay parameters support both serum/plasma and urine extended ranges 3x the upper measuring interval.

Using CH Diluent, 3-fold manual dilutions of 5 serum and 5 urine pools were made. Both the undiluted and diluted pools were processed with N=4 replicates; where the undiluted samples were auto-diluted on the Atellica CH system.

The serum/plasma and urine extended measuring interval is up to 4500 U/L.

Standardization

The Atellica® CH AMY_2 (AMY_2) assay is traceable to the IRMM/IFCC-456 reference material and commutable to the IFCC Alpha-Amylase Primary Reference Procedure as established by patient sample correlation.

Assigned values for calibrators are traceable to this standardization.

Conclusion

The Atellica® CH Amylase_2 (AMY_2) is substantially equivalent to the Roche Cobas Amylase Reagent in principle and performance based on the similarity of device designs and function demonstrated through method comparison and other performance attributes.