August 23, 2023

Ortho Clinical Diagnostics
Rebecca Lewis
Senior Regulatory Affairs Associate
Felindre Meadows
Pencoed
Bridgend, CF35 5PZ
United Kingdom

Re: K231517
Trade/Device Name: VITROS Immunodiagnostic Products CEA Reagent Pack
Regulation Number: 21 CFR 866.6010
Regulation Name: Tumor-Associated Antigen Immunological Test System
Regulatory Class: Class II
Product Code: DHX
Dated: May 23, 2023
Received: May 25, 2023

Dear Rebecca Lewis:

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,

Ying Mao -S

Ying Mao, Ph.D.
Branch Chief
Division of Immunology and Hematology Devices
OHT7: Office of In Vitro Diagnostics
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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K231517

Device Name
VITROS Immunodiagnostic Products CEA Reagent Pack

Indications for Use *(Describe)*
For In Vitro Diagnostic Use Only

For the quantitative measurement of carcinoembryonic antigen (CEA) concentration in human serum and plasma (EDTA or heparin) using the VITROS 5600 Integrated System, to aid in the prognosis and management of cancer patients in whom changing concentrations of CEA are observed.

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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510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.
The assigned 510(k) number is: K231517.

Submitter's Information

Ortho-Clinical Diagnostics Inc.

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Fax: (585) 453-3368
Contact Person: Rebecca Lewis

Preparation Date

Aug 23, 2023

Device Proprietary Name(s)

VITROS® Immunodiagnostic Products CEA Reagent Pack

Common Name(s) VITROS Immunodiagnostic Products CEA

Reagent Pack

Classification Names

Product Code	Class	Regulation Section	Panel
DHX	II	21 CFR 866.6010	Immunology

Predicate Device(s)

Predicate Device	FDA 510(k) Number
VITROS Immunodiagnostic Products CEA Reagent Pack	K041322

Device Description

The VITROS Immunodiagnostic Products CEA Reagent Pack (test) is performed using the VITROS CEA Reagent Pack and VITROS CEA Calibrators on the VITROS 5600 System.

An immunometric immunoassay technique is used, which involves the reaction of CEA present in the sample with a microwell coated with biotinylated Antibody (Mouse monoclonal anti-CEA) bound to Streptavidin, and a Horseradish Peroxidase (HRP)-labelled antibody conjugate (Mouse monoclonal anti- CEA). Unbound (HRP)-labeled anti-CEA antibody conjugate is removed by washing.

The bound HRP conjugate is measured by a luminescent reaction. A reagent containing luminogenic substrates (a luminol derivative and a peracid salt) and an electron transfer agent, is added to the wells. The HRP in the bound conjugate catalyzes the oxidation of the

luminol derivative, producing light. The electron transfer agent (a substituted acetanilide) increases the level of light produced and prolongs its emission. The light signals are read by the system. The amount of HRP conjugate bound is directly proportional to the concentration of CEA present in the sample.

VITROS CEA Reagent Pack contains:

1 reagent pack containing:

- 100 coated wells (antibody, mouse monoclonal anti-CEA, binds ≥8ng CEA/well);
- 9.7 mL assay reagent (buffer containing bovine serum albumin, bovine gamma globulin and antimicrobial agent).
- 9.7 mL conjugate reagent (HRP-mouse monoclonal anti-CEA, binds ≥123ng CEA/mL).

VITROS CEA Calibrator contains:

- 1 set of VITROS CEA Calibrators 1 and 2 (human CEA in bovine serum with antimicrobial agent, 2 mL); nominal values 3 and 250 ng/mL (µg/L)
- 16 calibrator bar code labels (8 for each calibrator)

Intended Use Statement(s):

Rx ONLY

For *in vitro* diagnostic use only.
For the quantitative measurement of carcinoembryonic antigen (CEA) concentration in human serum and plasma (EDTA or heparin) using the VITROS 5600 Integrated System, to aid in the prognosis and management of cancer patients in whom changing concentrations of CEA are observed.

Comparison to Predicate Devices

The following table provides a summary of the key features of the new device assessed against the predicate.

Device Characteristic	Predicate Device VITROS Immunodiagnostic Products CEA Reagent Pack, K041322, cleared 17 June 2004	Modified Device VITROS Immunodiagnostic Products CEA Reagent Pack
Intended Use	Rx ONLY For *in vitro* diagnostic use only. For the quantitative measurement of carcinoembryonic antigen (CEA) concentration in human serum and plasma (EDTA or heparin) using the VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems, to aid in the prognosis and management of cancer patients in whom changing concentrations of CEA are observed.	Rx ONLY For *in vitro* diagnostic use only. For the quantitative measurement of carcinoembryonic antigen (CEA) concentration in human serum and plasma (EDTA or heparin) using the VITROS 5600 Integrated System, to aid in the prognosis and management of cancer patients in whom changing concentrations of CEA are observed.
Antibody	Mouse Monoclonal anti-CEA antibody.	Same.
Sample Type	Serum and Plasma.	Same.

Sample Volume	20 µL.	Same.
Traceability	Traceable to in-house reference calibrators which have been value assigned to correlate to another commercially available test with reference to the 1st International Preparation 73/601.	Same.
Measuring Range	Analytical Measuring Interval: 0.31–400 ng/mL (µg/L)	Analytical Measuring Interval: 0.31–400 ng/mL (µg/L) Extended Measuring Interval: 400 – 40,000 ng/mL (µg/L) Reportable Measuring Interval: 0.31 – 40,000 ng/mL (µg/L)
Detect on Limit	LOB: 0.06 ng/mL (µg/L) LOD: 0.31 ng/mL (µg/L)	LOB: 0.08 ng/mL (µg/L) LOD: Same. LOQ: 0.31 ng/mL (µg/L)
Calibrator Levels	2.	Same.
Instrumentation	VITROS 5600 Integrated System	Same.

Differences:

Assay Principle	Sandwich immunoassay	Sandwich immunoassay. In the modified CEA assay, the mouse anti- CEA antibody has been removed from the Biotin Reagent and coated directly onto the well. The modification to allow the biotinylated antibody capture conjugate to be pre- bound to the well, eliminates the risk of biotin interference.
Assay Reagent	0.5% BSA, no Tween 20 or EDTA.	The modified product utilizes the same capture and detection antibodies. The modified product includes the addition of 0.6% Tween 20, 25 mM EDTA and an increase in BSA concentration from 0.5% to 3% in the CEA assay reagent. These modifications have improved the CEA assay: • The purpose of BSA in the assay reagent formulation is to minimize matrix effects, reduce non-specific binding (NSB) and improve the stability of the biotin conjugate. Hemoglobin in samples may adsorb to the wells and introduce an additional peroxidase activity, resulting in elevated signals and therefore a positive bias. Increase in BSA concentration of the assay reagent reduces the NSB, and therefore addresses the hemoglobin interference with the current assay. Improvement to the serum/plasma equivalence which previously required a limitation on bias for EDTA in the previously cleared product IFU.

Nonclinical Performance

Several nonclinical tests were performed.

Stability Studies

Long term stability and on-board storage performance was evaluated consistent with methods based on CLSI EP25-A.

Long Term Stability: Four runs have been performed on each of 3 Lots at each time-point, monthly intervals, data supports a 52 week shelf-life.

On-board Stability: Three Lots of the VITROS CEA assay were stored opened refrigerated for up to 12 weeks. Four runs were performed on each Lot at each time-point for fresh and open, all results were acceptable and support the current claim of 8 weeks on-board stability.

Precision

Precision was evaluated consistent with CLSI document EP05-A3, *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition.* Four (4) precision fluids, covering the analytical measuring interval, were evaluated for performance. For one reagent lot, two (2) replicates of each precision fluid were run on two (2) occasions per day for twenty (20) days, for a total of 80 data points per fluid.

The data presented are a representation of test performance and are provided as a guideline. Variables such as sample handling and storage, reagent handling and storage, laboratory environment, and system maintenance can affect reproducibility of test results.

Product Claim

System	Mean CEA Conc.	Repeatability*		Within Lab**		No. of Obs.	No. of Days
		SD	%CV	SD	%CV		
5600	6.55	0.114	1.7%	0.175	2.7%	80	20
	41.4	0.58	1.4%	1.02	2.5%	80	20
	228	4.4	1.9%	6.2	2.7%	80	20
	390	4.6	1.2%	11.4	2.9%	80	20

*Repeatability (formerly called within-run precision) was determined using two replicates per run.
**Within Lab precision was determined using a single reagent lot and a single calibration.

Additional Precision Analysis Summary

Units = ng/mL (µg/L)												
Sample	N	Mean	Within-run *(Repeatability)*		Between-Run		Between-Day		Between-Lot		Within-Laboratory*	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
PP1	240	6.44	0.107	1.7%	0.096	1.5%	0.095	1.5%	0.132	2.1%	0.217	3.4%
PP2	240	40.8	0.59	1.5%	0.84	2.1%	0.62	1.5%	0.45	1.1%	1.28	3.1%
PP3	240	223	4.3	1.9%	3.4	1.5%	3.2	1.4%	4.5	2.0%	7.8	3.5%
PP4	240	381	5.6	1.5%	6.6	2.1%	6.0	1.6%	8.7	2.3%	13.7	3.6%

*Within-laboratory precision includes following components: repeatability, between-run, between-day and between-lot was determined using three reagent lots.

Detection Capability

Detection studies for the VITROS CEA Reagent were evaluated consistent with CLSI document EP17-A2, *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline* – Second Edition. Four endogenous fluids containing no measurable carcinoembryonic antigen (CEA) were used for determining the LoB. The study design was 2 replicates per run, 2 runs per day over 5 test days = 20 reps per test fluid x 4 fluids = 80 replicates x 3 lots = 240 total replicates.

Five samples were used for establishing the LoD, which were targeted at 1 to 5 times the LoB concentration. The LoD samples were admixtures of serum samples containing endogenous CEA combined with CEA affinity stripped serum to achieve the approximate target CEA concentrations. The LoD fluids were used to determine the LoQ. All samples were run using three reagent lots on one VITROS 5600 System, 6 replicates per run, 2 runs per day over 5 test days = 60 reps per fluid x 5 fluids = 300 replicates x 3 lots = 900 total replicates.

The observed Limit of Detection (LoD) for the VITROS CEA test is 0.15 ng/mL (µg/L), determined consistent with CLSI document EP17. This supports the claimed LOD of 0.31ng/ml. The Limit of Quantitation (LoQ) for the VITROS CEA test was designed to be less than or equal to currently claimed low end of the measuring range of 0.31 ng/mL (µg/L) at 20% CV. The observed LoQ at 20% CV was determined to be 0.15 ng/mL (µg/L), consistent with CLSI document EP17. The claimed LoQ is set at 0.31 ng/mL (µg/L). The representative LoB is 0.08 ng/mL.

Linearity

Linearity studies were performed according to CLSI document EP06 2nd edition. In a study with 13 levels and five replicates for each level on 1 reagent lot on one VITROS 5600 Integrated System, linearity was demonstrated from 0.22 ng/mL (ug/L) to 500 ng/mL (ug/L) with deviations from linearity within +/- 14.3%.

		Slope		Intercept		
Dilution Range	**% Recovery**	**Estimate**	**95% CI**	**Estimate**	**95% CI**	**R^2**
0.22 to 500	82.1% to 109%	1.04275	1.025 to 1.061	-0.06678	-0.085 to -0.049	0.999

Regression			Predicted value = 1.04275 (Expected Value) -0.06678					
Sample ID	**% HP**	**Expected value (ng/mL)**	**Measured Value (ng/mL)**	**Predicted Value (ng/mL)**	**Deviation (ng/mL)**	**% Deviation**	**Allowable nonlinearity**	**Within Allowable nonlinearity**
Lin-2	0.04	0.267	0.219	0.212	0.008	3.6%	±14.3%	Yes
Lin-3	0.05	0.317	0.262	0.264	-0.002	-0.8%	±14.3%	Yes
Lin-4	0.50	2.565	2.632	2.608	0.024	0.9%	±14.3%	Yes
Lin-5	1.01	5.11	5.26	5.26	-0.006	-0.1%	±14.3%	Yes
Lin-6	5.00	25.0	26.2	26.0	0.19	0.7%	±14.3%	Yes
Lin-7	14.99	74.95	81.6	78.1	3.48	4.5%	±14.3%	Yes
Lin-8	34.98	175	186	182	4.2	2.3%	±14.3%	Yes
Lin-9	50.00	250	266	260	5.4	2.1%	±14.3%	Yes
Lin-10	69.99	350	351	365	-13.6	-3.7%	±14.3%	Yes
Lin-11	80.00	400	398	417	-18.3	-4.4%	±14.3%	Yes
Lin-12	89.96	449	455	469	-13.4	-2.9%	±14.3%	Yes
Lin-13	100.00	500	500	521	-21.3	-4.1%	±14.3%	Yes

Linearity/Measuring Range

VITROS System	Measuring (Reportable) Range
5600	0.31–400 ng/mL(µg/L)

The extended measuring interval is 400–40,000 ng/mL (µg/L).
Results with concentrations greater than 40,000 ng/mL (µg/L) will be reported as >40,000 ng/ mL(µg/L).

Matrix Comparison

Serum and plasma (Li-Hep and EDTA) specimen matrices was determined to be equivalent.
The results met the acceptance criteria for the comparison between serum and plasma (Li-Hep and EDTA) specimens spanning the expected measuring interval. Based on the analysis serum and plasma (Li-Hep and EDTA) are suitable specimen matrices for use with the VITROS CEA assay.

Specimens Recommended

- Serum and Plasma

Specimens Not Recommended.

- Do not use turbid specimens. Turbidity in specimens may affect test results.

VITROS 5600 System		
Ordinary Deming	**Li-Hep**	**EDTA**
Slope	0.998	0.995
95% CI (Slope)	0.9765 to 1.019	0.9459 to 1.044
Intercept	-0.1177	-0.8768
95% CI (Intercept)	-0.8353 to -0.5999	-3.056 to 1.302
Correlation Coefficient (r)	0.999	0.998
n	40	40
Pass/Fail Status	Pass	Pass

Analytical Specificity

Known Interferents

The VITROS CEA assay was screened for interfering substances at CEA concentrations of approximately 3.00 ng/mL(µg/L) and 15.0 ng/mL(µg/L) following EP07 3rd ed – Interference Testing in Clinical Chemistry and EP37 1st ed – Supplemental Tables for Interference Testing in Clinical Chemistry. Commonly encountered substances were tested. Of the compounds tested, none were found to cause bias of >10%.

For substances that were tested and did not interfere, refer to "Substances that do not Interfere."

Substances that do not Interfere

The substances listed in the table below were tested with the VITROS CEA test following CLSI EP07and EP37 and found not to cause bias > 10% at CEA concentrations of approximately 3.00 ng/mL(µg/L) and 15.0 ng/mL(µg/L) at the test concentrations shown.

Substance	Concentration
Acetaminophen	20.3 mg/dL
N-Acetylcysteine	15.0 mg/dL
Acetylsalicylic acid	50 mg/dL
Alpha-tocopherol	6.45 mg/dL
Aminoglutethimide	39.8 mg/dL
Amoxicillin	5.40 mg/dL
Ascorbic acid	6.00 mg/dL
Bilirubin, conjugated	100 mg/dL
Bilirubin, unconjugated	100 mg/dL
Biotin	0.351 mg/dL
Bleomycin	300 mg/dL

Carbamazepine	4.50 mg/dL
Cefoxitin sodium	695 mg/dL
Cholecalciferol (D3)	19.2 µg/dL
Cholesterol	400 mg/dL
Cisplatin	1.3 mg/dL
Codeine	0.141 mg/dL
Cotinine	0. 24 mg/dL
Cyclophosphamide	54.9 mg/dL
Dextran 40	1200 mg/dL
Dextromethorphan	0.00156 mg/dL
Doxorubicin hydrochloride	5.2 mg/dL
Enoxaparin	360 U/dL
Ethanol	600 mg/dL
Etoposide	83 mg/dL
5-Fluorouracil	34.8 mg/dL
Furosemide	1.59 mg/dL
Gamma globulin	6 g/dL
HAMA (Human Anti-Mouse Antibodies)	800 µg/L
Hemoglobin	1000 mg/dL
Hydralazine	1.44 mg/dL
Hydrocodone	0.0072 mg/dL
Ibuprofen	71.0 mg/dL
Intralipid	2000 mg/dL
Levothyroxine	0.0429 mg/dL
Loratadine	0.0087 mg/dL
Methotrexate	136 mg/dL
Mitomycin C	5.52 mg/dL
Morphine	0.78 mg/dL
Naproxen	36.0 mg/dL
Omeprazole	0.840 mg/dL
Phenytoin	6.00 mg/dL
Prednisone	0.010 mg/dL
Rheumatoid Factor	900 IU/mL
Tamoxifen	4.8 mg/dL
Theophylline	6.0 mg/dL
Total protein	15.0 g/dL
Triglycerides	1500 mg/dL
Vancomycin hydrochloride	12.3 mg/dL
Vinblastine	138 mg/dL
Vincristine	140 mg/dL

Cross-Reactivity

The cross-reactivity of the VITROS CEA test was evaluated by adding the following substance to a sample containing no CEA.

Substance	Tested Concentration	VITROS 5600 % Cross Reactivity		
		Master Lot 9991	Master Lot 9992	Master Lot 9993
Non- specific Cross- reacting Antigen 1 (NCA 1)	500 ng/mL (µg/L)	ND	ND	ND

ND = Not Detectable; mean result is below the measuring interval of the assay

Other Limitations

- The VITROS CEA test is not recommended as a screening procedure for cancer detection.
- Patients with confirmed carcinoma frequently have CEA levels in the same range as normal patients. Elevated levels of CEA may be found in smokers or patients with non-malignant conditions. Based on these observations, CEA levels in serum and plasma, regardless of level, should not be interpreted as absolute evidence of the presence or absence of malignant disease.
- Certain drugs and clinical conditions are known to alter CEA concentrations in vivo. For additional information, refer to one of the published summaries.
- The results from this test should be used and interpreted only in the context of the overall clinical picture.
- Heterophile, as well as human anti-animal antibodies (most common being human anti-mouse antibodies or HAMA) in serum or plasma of certain individuals are known to cause interference with immunoassays. The anti-animal antibodies may be present in blood samples from individuals regularly exposed to animals or who have received preparations of mouse monoclonal antibodies for diagnosis or therapy. Results inconsistent with clinical observations indicate the need for additional testing.

Dilution

The dilution recovery and dilution imprecision product requirements were met for the VITROS Immunodiagnostic Products CEA Reagent Pack. Serum or Plasma (EDTA or heparin) samples with concentrations greater than the measuring range will be reported as >400 ng/mL(µg/L) and may be automatically diluted on the system up to 100-fold (1 part sample with 99 parts diluent) by the VITROS 5600 Integrated System with the VITROS High Sample Diluent B Reagent Pack prior to test. Refer to the VITROS High Sample Diluent B Reagent Pack Instructions for Use.

Expected Values

Adult Reference Interval

The adult reference interval was validated following CLSI document EP28-A3c *Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline* – Third Edition.

The distribution of CEA values for healthy non-smokers (n=68) and healthy smokers (n=72) showed equivalency to the expected values claim published in the Instructions for Use of the current US VITROS CEA

assay, therefore the current distribution of results for healthy subjects will be transferred to the updated VITROS CEA assay.

Product Claim:

Category	N	Percent (%)			
		0-3.0 ng/mL (µg/L)	>3.0-5.0 ng/mL (µg/L)	>5.0-10.0 ng/mL (µg/L)	>10.0 ng/mL (µg/L)
Healthy Subjects					
Nonsmokers	149	91.9	6.0	0.7	1.3
Smokers	101	67.3	22.8	8.9	1.0
Total	250	82.0	12.8	4.0	1.2

Distribution of Healthy Subjects Results for the updated VITROS CEA assay:

Category	n	Percent (%)			
		0-3.0 ng/mL (µg/L)	>3.0-5.0 ng/mL (µg/L)	>5.0-10.0 ng/mL (µg/L)	>10.0 ng/mL (µg/L)
Healthy Subjects					
Nons-mokers	68	89.7	7.4	2.9	0
Smokers	72	72.2	22.2	5.6	0

High Dose Hook

The assessment was consistent with the high dose hook guidance found in CLSI document EP34. The high dose hook panel was prepared with VITROS High Sample Diluent B (HSDB), containing no measurable CEA, spiked with endogenous CEA antigen to produce a fluid with a concentration of approximately 546,000 ng/mL(µg/L). This fluid was diluted with VITROS HSDB to produce a set of ten fluids (the High Dose Hook Panel) with concentrations spanning between 273 and 546,000 ng/mL (µg/L). The high dose hook panel samples were tested in singleton using one reagent lot on one VITROS 5600 System.

The updated VITROS CEA assay has a high dose hook claim of up to 80,000ng/mL.

Traceability of Calibration

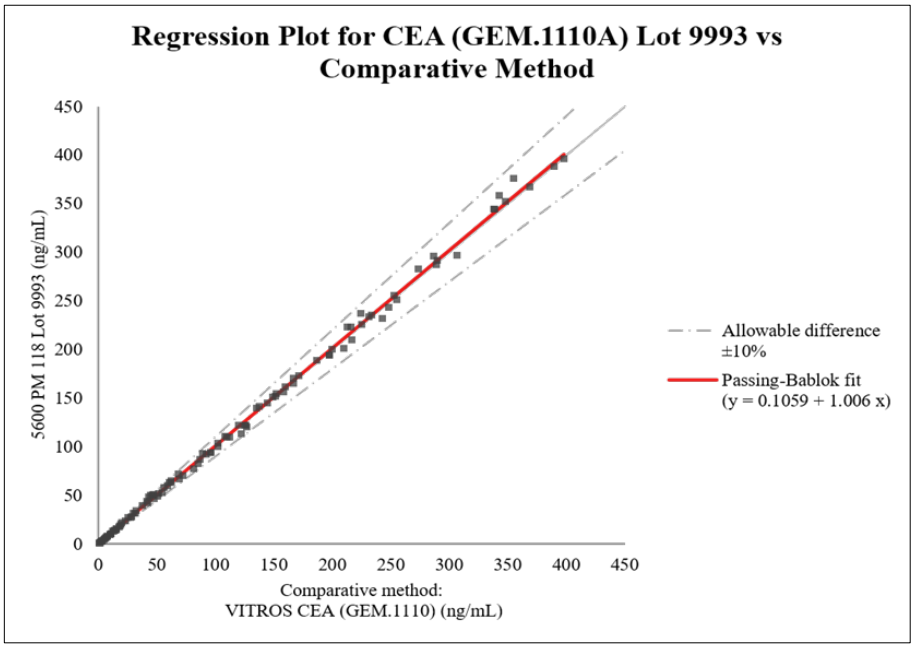
The Calibration of the VITROS CEA assay is traceable to in-house reference calibrators which have been value assigned to correlate to another commercially available test with reference to the 1st International Preparation 73/601.

Method Comparison

Accuracy was evaluated consistent with CLSI documents *Measurement Procedure Comparison and Bias Estimation Using Patient Samples. 3rd ed. CLSI guideline* EP09c; and *Evaluation of Total Analytical Error for Quantitative medical laboratory Measurement Procedures.* 2nd ed. CLSI guideline EP21. Human serum samples were obtained from certified vendors and tested neat. A total of 110 samples were tested in singleton using one reagent lot and one VITROS 5600 Integrated System.

Accuracy was evaluated consistent with CLSI document EP09c. The plot and table show the results of a method comparison study using patient (serum) samples analyzed on the VITROS CEA assay

compared with those analyzed on the VITROS CEA assay (K041322) on the VITROS 5600 Integrated System. The relationship between the 2 methods was determined by a Passing and Bablok regression as shown in the Figure below.



System	n	Slope (95% CI)	Correlation Coefficient	Conventional Units (U/mL)	
				Range of Samples	Intercept (95% CI)
5600 vs. Comparative Method	110	1.01 (0.9972 to 1.012)	0.999	0.56-396	0.106 (-0.01602 to -0.3729)

Conclusion

The conclusions drawn from the nonclinical tests (discussed above) demonstrate the updated VITROS Immunodiagnostic Products CEA Reagent pack is as safe, effective, and performs as well as the cleared predicate device. The information submitted in the premarket notification is complete and supports a substantial equivalence decision.