August 28, 2024

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

Re: K241534
Trade/Device Name: VITROS Immunodiagnostic Products Syphilis Reagent Pack
Regulation Number: 21 CFR 866.3830
Regulation Name: Treponema Pallidum Treponemal Test Reagents
Regulatory Class: Class II
Product Code: LIP
Dated: May 30, 2024
Received: May 30, 2024

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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device"

(https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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,

Himani Bisht -S

Himani Bisht, Ph.D
Assistant Director
Viral Respiratory and HPV Branch
Division of Microbiology 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: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K241534

Device Name
VITROS Immunodiagnostic Products Syphilis Reagent Pack (VITROS Syphilis test)

Indications for Use *(Describe)*
VITROS Immunodiagnostic Products Syphilis Reagent Pack (VITROS Syphilis test)

For the qualitative determination of total (IgG and IgM) antibodies to Treponema pallidum (TP) specific antigens in human serum and plasma using the VITROS 5600 Integrated System.

The presence of antibodies to Treponema pallidum (TP) specific antigens, in conjunction with non-treponemal laboratory tests and clinical findings may aid in the diagnosis of syphilis infection.

The VITROS Syphilis test is not intended for blood and tissue donor screening.

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: K241534.

Submitter's Information

Ortho Clinical Diagnostics

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Pencoed,

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Fax: 585-453-4110
Contact Person: Rebecca Lewis

Preparation Date

August 27, 2024

Device Proprietary Name(s)

VITROS Immunodiagnostic Products Syphilis Reagent Pack

Common Name(s) VITROS Syphilis test

Classification Names

Product Code	Class	Regulation Section	Panel
LIP	II	21 CFR 866.3830 Division of Microbiology Devices (DMD)	Microbiology

Predicate Device(s)

Predicate Device	FDA 510(k) Number
Elecsys Syphilis	K160910 & K211302

Device Description

The VITROS Immunodiagnostic Products Syphilis test is performed using the VITROS Immunodiagnostic Products Syphilis Reagent Pack and VITROS Immunodiagnostic Products Syphilis Calibrator on the VITROS 5600 Integrated System.

An immunometric technique is used; this involves a two-stage reaction. In the first stage antibodies to Syphilis TP specific antigens present in the sample bind with biotinylated recombinant Syphilis TP antigens immobilized on streptavidin coated wells. Unbound sample is removed by washing. In the second stage conjugate reagent containing horseradish peroxidase (HRP)-labeled recombinant Syphilis TP antigens is added. The conjugate binds specifically to any antibody to Syphilis TP specific antigens captured on the well in the first stage. Unbound 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.

VITROS Immunodiagnostic Products Syphilis Reagent Pack contains:

1 reagent pack containing:

- 100 coated wells; biotin-recombinant Syphilis TP antigens, 0.15 µg/mL.
- 13.1 mL assay reagent (buffer with bovine gamma globulin, bovine serum albumin and antimicrobial agent).
- 20.4 mL conjugate reagent (HRP-recombinant Syphilis TP antigens, 0.15 µg/mL) in buffer with bovine serum albumin and antimicrobial agent.

VITROS Syphilis Calibrator contains:

- 1 vial of VITROS Syphilis Calibrator (human anti-Syphilis TP antigen in anti-Syphilis TP antigen negative human plasma with antimicrobial agent, 2.2 mL).

Intended Use Statement(s):

VITROS Immunodiagnostic Products Syphilis Reagent Pack (VITROS Syphilis test)
For the qualitative determination of total (IgG and IgM) antibodies to *Treponema pallidum* (TP) specific antigens in human serum and plasma using the VITROS 5600 Integrated System.

The presence of antibodies to *Treponema pallidum* (TP) specific antigens, in conjunction with non-treponemal laboratory tests and clinical findings may aid in the diagnosis of syphilis infection.

The VITROS Syphilis test is not intended for blood and tissue donor screening.

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 Roche Elecsys Syphilis assay, K160910 and K211302, cleared 28 July 2016 and 20 July 2021	New Device VITROS Immunodiagnostic Products Syphilis Reagent Pack
Intended Use	For the *in vitro* qualitative detection of total antibodies (IgGand IgM) to *Treponema pallidum* in human serum and plasma. The test is intended as an aid in the diagnosis of syphilis infection in conjunction with clinical signs and symptoms. The Elecsys Syphilis immunoassay is not intended for use in screening blood or tissue donors. The effectiveness of this assay in testing blood or tissue donors has not been established. The electrochemiluminescence immunoassay "ECLIA" is intended for use on cobas e immunoassay analyzers.	VITROS Immunodiagnostic Products Syphilis Reagent Pack (VITROS Syphilis test) For the qualitative determination of total (IgG and IgM) antibodies to *Treponema pallidum* (TP) specific antigens in human serum and plasma using the VITROS 5600 Integrated System. The presence of antibodies to *Treponema pallidum* (TP) specific antigens, in conjunction with non-treponemal laboratory tests and clinical findings may aid in the diagnosis of syphilis infection. The VITROS Syphilis test is not intended for blood and tissue donor screening.
Basic Principle	Sandwich immunoassay.	Same.
Analyte	Anti-Syphilis TPA.	Same.
Sample Type	Serum and Plasma.	Same.
Automated	Automated assay.	Same.
Measurement	Qualitative.	Same.
Interpretation of results	Samples with a cutoff index < 1.00 are non-reactive. These samples are considered negative for *anti-Treponema pallidum* antibodies. Samples with a cutoff index ≥ 1.00 are considered reactive.	Same.

General Device Characteristic Differences:

Traceability	N/A.	Traceable to an in-house reference calibrator which has been value assigned to optimize clinical sensitivity and specificity.
Sample Volume	6 µL.	25 µL.
Calibrator Levels	2.	1.

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, will support a 52 week shelf-life. All results were acceptable and support a claim of 21 weeks stability currently.

On-board Stability: Three Lots of the VITROS Immunodiagnostic Products Syphilis reagent pack were stored opened refrigerated for up to 13 weeks. Four runs were performed on each Lot at each time-point for fresh and open, all results were acceptable and support a claim of 12 weeks on-board stability.

Result Calculation

$$\text{Result} = \frac{\text{Signal for test sample}}{\text{Signal at Cutoff (Cutoff value)}}$$

Interpretation of results

Samples with results less than 1.00 will be flagged as "Non-reactive" and samples with results greater than or equal to 1.00 will be flagged as "Reactive".

VITROS Syphilis Test Result (S/C)	Status	Interpretation
< 1.00	Non-reactive	Indicates no active or previous infection with *Treponema pallidum*.
≥ 1.00	Reactive	Indicates active or previous infection with *Treponema pallidum*.

Note: The results from this or any other diagnostic test should be used and interpreted only in the context of the overall clinical picture. A Non-reactive test result does not exclude the possibility of recent exposure to *Treponema pallidum*. Levels of anti-*T.pallidum* antibodies may be below the cutoff in early infection.

Precision

The within-laboratory precision of the VITROS Syphilis test was evaluated with five serum pools (PP) following CLSI document EP05. [15] Two reagent lots and calibrator lots were included in the study. For each reagent lot, operators ran two replicates of each precision pool on two occasions per day for 20 non-consecutive days.

The data presented are a representation of assay 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 assay results.

Product Claim

Panel Member	No. of Obs	% Reactive	Grand Mean	Repeatability* (Within Run)		Between-Run		Between-Day		Between-Lot		Within-Laboratory**	
				SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Human Serum Pool, Non-reactive	160	0% (0/160)	0.02	0.003	–	0.001	–	0.001	–	0.002	–	0.004	–
Human Serum Pool, High Non-reactive	160	0% (0/160)	0.72	0.016	2.2	0.040	5.5	0.015	2.1	0.127	17.7	0.135	18.8
Human Serum Pool, Low Reactive	160	100% (160/160)	1.27	0.026	2.0	0.053	4.2	0.038	3.0	0.199	15.7	0.211	16.6
Human Serum pool, Reactive	160	100% (160/160)	2.16	0.041	1.9	0.064	2.9	0.062	2.8	0.300	13.9	0.315	14.6
Human Serum Pool, Reactive	160	100% (160/160)	7.70	0.130	1.7	0.080	1.0	0.220	2.8	0.889	11.5	0.928	12.0

*Repeatability was determined using two replicates per run.

** Within-Laboratory precision variability contains the Within Run, Between Run, Between Day and Between Lot variance components using two individual reagent lots with a single calibration for each reagent lot.

Reproducibility

A five-level reproducibility panel was tested with one lot of reagents at three sites, twice a day, with two unique operators a day, three replicates per run, for a total of five testing days. The repeatability (within day), between run/operator, between day, between site, and reproducibility (total) precision estimates (CV (%)) derived from a variance component analysis are summarized below.

Product Claim

Panel Description	Mean VITROS Syphilis Results (S/C)	Repeatability[a] (Within Run)		Between Run/Operator[b]		Between Day[c]		Between Site[d]		Reproducibility[e]		N
		SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	
Human Serum Pool, Non-reactive	0.02	0.003	-	0.000	-	0.002	-	0.005	-	0.006	-	90
Human Serum Pool, High Non-reactive	0.75	0.021	2.8	0.018	2.4	0.019	2.5	0.015	2.0	0.037	4.9	90
Human Serum Pool, Low Reactive	1.29	0.036	2.8	0.024	1.9	0.038	3.0	0.024	1.8	0.062	4.9	90
Human Serum Pool, Reactive	2.14	0.048	2.2	0.030	1.4	0.047	2.2	0.047	2.2	0.088	4.1	90
Human Serum Pool, Reactive	7.42	0.145	2.0	0.000	0.0	0.080	1.1	0.246	3.3	0.297	4.0	90

[a] Repeatability: Variability of the VITROS Syphilis test performance within day replicate, calculated using data across all sites.

[b] Between Run/Operator: Variability of the VITROS Syphilis test performance from run to run, calculated using data across all sites.

[c] Between Day: Variability of the VITROS Syphilis test performance from day to day, calculated using data across all sites.

[d] Between site: Variability of the VITROS Syphilis test performance from site to site.

[e] Reproducibility (Total): Variability of the test incorporating factors of repeatability, between run/operator, between day, and between site.

Matrix Comparison

Serum and plasma (Heparin and EDTA) specimen matrices were determined to be equivalent. The results met the acceptance criteria for the comparison between serum and plasma (Heparin and EDTA) specimens spanning the expected measuring interval. Based on the analysis, serum and plasma (Heparin and EDTA) are suitable specimen matrices for use with the VITROS Immunodiagnostic Products Syphilis test.

Specimens Recommended

Verified specimen types to be used with this test:

- Serum
- Serum Separator Tube (SST)
- Plasma Separator Tube (PST)
- Lithium heparin plasma
- Sodium heparin plasma
- K2 EDTA plasma
- K3 EDTA plasma

Specimens Not Recommended

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

Sample Stability Studies

Samples were collected from in-house donors in the following tube types: serum, serum separator tubes (SST), LiHep plasma separator tubes (PST), lithium heparin (LiHep) plasma, sodium heparin (NaHep) plasma, K2 EDTA plasma and K3 EDTA plasma and were evaluated at room temperature (30 degrees Celsius), refrigerated (2 – 8 degrees Celsius), and frozen (minus 20 degrees Celsius) storage conditions. All samples were tested at every time point and storage condition. Room temperature time points included 24 hours and 7 days. Refrigerated time points included 3 and 7 days. Frozen time points included 7 days, 28 days and 28 days with five freeze-thaw cycles.

Ortho is claiming the following storage conditions for specimens.

Serum, Serum (SST), Serum (PST), Plasma (PST), Li-Heparin, Na-Heparin, K2 EDTA and K3EDTA at:

2 to 8°C for 7 days
Room temperature for 7 days
Frozen for 28 days
Samples may be frozen and thawed up to 5 times.

Carryover

A carryover study was executed which verified that the VITROS Immunodiagnostic Products Syphilis test is not affected by sample carry over.

Detection of Syphilis IgG and IgM

A study was conducted to evaluate the ability of the VITROS Immunodiagnostic Products Syphilis test to detect Syphilis TPA specific IgM and IgG antibodies. The VITROS Immunodiagnostic Products Syphilis reagent pack is capable of specifically detecting syphilis IgG and IgM antibodies.

Analytical Specificity

Substances that do not Interfere

The VITROS Syphilis test was evaluated for potential interference consistent with CLSI documents EP07 [16] and EP37. [17] Commonly encountered substances were tested using two lots of reagents. Of the compounds tested, none was found to interfere with the clinical interpretation of the assay at the concentrations indicated when tested in negative and weakly reactive samples.

Substance	Concentration	
	Conventional Units	SI Units
Acetaminophen	15.6 mg/dL	1030 µmol/L
Acetylcysteine	15 mg/dL	920 µmol/L
Acetylsalicylic Acid	3.0 mg/dL	167 µmol/L
Ampicillin-Na	7.5 mg/dL	215 µmol/L
Ascorbic Acid	30.6 mg/dL	1738 µmol/L
Bilirubin (conjugated)	40.0 mg/dL	475 µmol/L
Bilirubin (unconjugated)	40.0 mg/dL	684 µmol/L
Biotin	3510 ng/mL	14.3 µmol/L
Cefoxitin	660 mg/dL	15500 µmol/L
Cholesterol	400 mg/dL	10.3 mmol/L
Cyclosporine	0.18 mg/dL	1.50 µmol/L
Doxycyclin	18 mg/L	40.5 µmol/L
Hemoglobin	1000 mg/dL	10 g/L
Heparin	330 U/dL	330 units/dL
Human anti-mouse Antibodies (HAMA)	5120 ng/mL	N/A
Ibuprofen	21.9 mg/dL	1060 µmol/L
Human IgG	2894 mg/dL	N/A
Intralipid	2000 mg/dL	NA
Levodopa	0.75 mg/dL	38 µmol/L
Methyldopa	2.25 mg/dL	107 µmol/L
Metronidazole	123 mg/L	7190 µmol/L
Phenylbutazone	32.1 mg/dL	1040 µmol/L
Total Protein	15 g/dL	150 g/L
Rheumatoid Factor	2941 IU/mL	N/A
Rifampicin	4.8 mg/dL	58.3 µmol/L
Sodium Azide	20 mg/dL	3076 µmol/L
Theophylline	60 mg/L	333 µmol/L
Triglycerides	1500 mg/dL	16.94 mmol/L

NA = Not Applicable (alternate units not provided)

Cross-Reactivity

The cross-reactivity of the VITROS Immunodiagnostic Products Syphilis test was evaluated for potential cross-reactivity in anti-syphilis TP negative samples from medical conditions unrelated to syphilis infection. The results are summarized in the table below.

Sample Category	Number of Samples	Non-reactive	Reactive
Anti-nuclear antibodies (ANA)	10	10	0
Borrelia burgdorferi infection IgG (European and US strains)	10	10	0
Cytomegalovirus (anti-CMV IgG positive and IgM positive)	10	10	0
Epstein-Barr Virus (EBV IgG positive and IgM positive)	10	10	0
Hepatitis A (HAV) IgG and IgM	10	10	0
Hepatitis B (HBV) IgG and IgM	10	10	0
Hepatitis C (HCV) IgG and IgM	10	10	0
Herpes Simplex Virus 1/2 (anti-HSV-1/2 IgG positive and IgM positive)	10	10	0
Human Immunodeficiency Virus (HIV 1/2) IgG and IgM	12	10	2*
Rheumatoid Arthritis/Rheumatoid Factor	10	10	0
Rubella IgG and IgM	10	10	0
Hyperglobulinemia	10	10	0
Systemic Lupus Erythematosus (SLE)	10	10	0
Toxoplasmosis IgG positive and IgM positive	10	10	0
Varicella-Zoster Virus (VZV IgG positive)	15	10	5*
E. coli antibodies	10	10	0
Leptospirosis	10	10	0
VCA (EBV Viral Capsid Antigen) IgM	10	10	0

* The 7 samples that were reactive with the VITROS Syphilis test were confirmed as coinfected and positive for anti-*Treponema pallidum* antibodies with another syphilis total antibody assay. No cross-reactivity was observed.

Limitations of the Procedure

- A reactive test result for treponemal antibodies is not diagnostic of syphilis without additional serologic testing and a full clinical evaluation.
- False reactive results can be expected with any test kit. The proportion of these falsely reactive specimens is dependent upon the specificity of the test kit, specimen integrity, and the characteristics of the local population being screened.
- Results in samples from immunosuppressed patients or from patients with disorders leading to

immunosuppression should be interpreted with caution.

- The detection of treponemal antibodies may indicate recent, past, or successfully treated syphilis. This test cannot distinguish between active and treated infection, and therefore may not be used to determine response to therapy, relapse, or reinfection.
- Assay interference due to circulating antibodies against yaws, pinta, and bejel has not been evaluated. Cross-reactivity with these treponemal disease conditions is to be expected with treponemal antibody tests.
- A Non-reactive test result does not completely rule out the possibility of an infection with Treponema pallidum. Serum or plasma samples from the very early (pre-seroconversion) phase or the late phase of a syphilis infection can occasionally yield negative findings.
- Heterophilic antibodies in serum or plasma samples may cause interference in immunoassays. These antibodies may be present in blood samples from individuals regularly exposed to animals or who have been treated with animal serum products. Results which are inconsistent with clinical observations indicate the need for additional testing.
- Certain drugs and clinical conditions are known to alter antibody concentrations in vivo. For additional information, refer to one of the published summaries.
- Do not use quality control materials preserved with azide.

Traceability of Calibration

Calibration of the VITROS Immunodiagnostic Products Syphilis reagent pack is traceable to an in-house reference calibrator which has been value assigned to optimize clinical sensitivity and specificity.

Clinical Studies

Clinical Performance in Prospectively Collected Specimens

A total of 924 prospective specimens from the intended use population collected from 6 sites in the United States were tested at 3 sites using the VITROS Syphilis test, including 615 subjects sent for routine syphilis testing, 47 pregnant women and 262 HIV positive subjects. In addition, all samples were tested according to a composite testing algorithm using FDA-cleared tests that included a treponemal electrochemiluminescence immunoassay (TP-ECLIA), a Rapid Plasma Reagin (RPR) non-treponemal assay and aTreponema pallidum Particle Agglutination (TP-PA) Treponema-specific assay.

A summary of the serological test profile for all prospectively collected specimens in the intended use population is presented in the following table.

Serological Test Profile for the Prospective Intended Use Population

TP-ECLIA Result	RPR Result	TP-PA Result	Final Comparator Result	VITROS Syphilis Result	Number of Subjects
Non-reactive	Non-reactive	N/A*	Negative	Non-reactive	684
				Reactive	2
Non-reactive	Reactive	Reactive	Positive	Non-reactive	1
				Reactive	0
		Non-reactive	Negative	Non-reactive	2
				Reactive	1
		Inconclusive	Negative	Non-reactive	0
				Reactive	0
Reactive	Reactive	N/A*	Positive	Non-reactive	0
				Reactive	84
Reactive	Non-reactive	Reactive	Positive	Non-reactive	0
				Reactive	129
		Non-reactive	Negative	Non-reactive	2
				Reactive	14
		Inconclusive	Positive	Non-reactive	0
				Reactive	5

* N/A = Test not performed

The comparison between the VITROS Syphilis results and the final comparator results for the prospective specimens in the intended use population is shown in the following table.

VITROS Syphilis Test Results Compared with Final Comparator for the Prospective Intended Use Population

VITROS Syphilis	Final Comparator Results		Total
	Positive for Syphilis	Negative for Syphilis	
Reactive	218	17	235
Non-reactive	1	688	689
Total	219	705	924

The positive percent agreement (PPA) and the negative percent agreement (NPA) between the VITROS Syphilis results and the final comparator results for each subgroup of the prospectively collected specimens in the intended use population are summarized in the following table.

Percent Agreement by Category for the Prospective Intended Use Population

Subgroup	PPA % (n/N)	95% CI* (%)	NPA % (n/N)	95% CI* (%)
Routine Syphilis**	98.8 (83/84)	93.6 - 99.8	99.2 (527/531)***	98.1 - 99.7
Pregnant Women	100.0 (1/1)	20.7 - 100.0	97.8 (45/46)***	88.7 - 99.6
HIV Positive	100.0 (134/134)	97.2 - 100.0	90.6 (116/128)***	84.3 - 94.6
All Prospective Subgroups	99.5 (218/219)	97.5 - 99.9	97.6 (688/705)***	96.2 - 98.5

*95% Wilson score confidence interval
**Does not include prospectively collected Pregnant Women and HIV Positive specimens
***Of the 17 discordant samples that were negative by the Final Comparator, 14 samples (2 routine Syphilis, 1 pregnancy, 11 HIV positive) were reactive by a FDA cleared *Treponema pallidum* antibody test.

Clinical Performance in Retrospective Specimens

A total of 547 retrospective purchased samples were tested at 3 sites using the VITROS Syphilis test, including 243 samples from pregnant women, 152 HIV positive samples and 152 pre-selected positive samples. In addition, all samples were tested according to a composite testing algorithm using FDA-cleared tests that included treponemal electrochemiluminescence immunoassay (TP-ECLIA), a Rapid Plasma Reagin (RPR) non-treponemal specific assay and a *Treponema-pallidum* Particle Agglutination (TP-PA) Treponema-specific assay.

The comparison between the VITROS Syphilis results and the final comparator results for the retrospective specimens is shown in the following table.

VITROS Syphilis Test Results Compared with Final Comparator for the Retrospective Specimens

VITROS Syphilis	Final Comparator Results		Total
	Positive for Syphilis	Negative for Syphilis	
Reactive	213	4	217
Non-reactive	0	330	330
Total	213	334	547

The PPA and the NPA between the VITROS Syphilis results and the final comparator results for each subgroup of the retrospective specimens are summarized in the following table.

Percent Agreement by Category for the Retrospective Specimens

Subgroup	PPA % (n/N)	95% CI* (%)	NPA % (n/N)	95% CI* (%)
Pregnant Women	100.0 (31/31)	89.0 - 100.0	100.0 (212/212)	98.2 - 100.0
HIV Positive	100.0 (30/30)	88.6 - 100.0	96.7 (118/122)**	91.9 – 98.7
Pre-selected Positive	100.0 (152/152)	97.5 - 100.0	N/A***	N/A***

*95% Wilson score confidence interval
**Four discordant samples that were negative by the Final Comparator were reactive by a FDA cleared *Treponema pallidum* antibody test.
***N/A = Not applicable, denominator is zero

Clinical Performance in Pregnant Women

Samples from 290 pregnant women were tested in the study. Of these samples, 47 were prospectively collected and 243 were retrospective samples. The percent agreement between the VITROS Syphilis results and the final comparator results is shown below stratified by pregnancy trimesters.

Percent Agreement for the Pregnant Women Population

Pregnant Women	PPA % (n/N)	95% CI* (%)	NPA % (n/N)	95% CI* (%)
Prospectively Collected Specimens				
First Trimester	100.0 (1/1)	20.7 - 100.0	96.0 (24/25)**	80.5 - 99.3
Second Trimester	N/A***	N/A***	100.0 (19/19)	83.2 - 100.0
Third Trimester	N/A***	N/A***	100.0 (2/2)	34.2 - 100.0
Overall Prospectively Collected Specimens	100.0 (1/1)	20.7 - 100.0	97.8 (45/46)**	88.7 - 99.6
Retrospective Specimens				
First Trimester	N/A***	N/A***	100.0 (42/42)	91.6 - 100.0
Second Trimester	100.0 (31/31)	89.0 - 100.0	100.0 (102/102)	96.4 - 100.0
Third Trimester	N/A***	N/A***	100.0 (68/68)	94.7 - 100.0
Overall Retrospective Specimens	100.0 (31/31)	89.0 - 100.0	100.0 (212/212)	98.2 - 100.0

*95% Wilson score confidence interval
**One discordant sample that was negative by the Final Comparator was reactive by a FDA cleared *Treponema pallidum* antibody test.
***N/A = Not applicable, denominator is zero

Clinical Performance in HIV Positive Individuals

Samples from 414 HIV positive individuals were tested in the study. Of these samples, 262 were prospectively collected and 152 were retrospective samples. The percent agreement between the VITROS Syphilis results and the final comparator results is shown below.

Percent Agreement for the HIV Positive Population

HIV Positive Specimens	PPA % (n/N)	95% CI* (%)	NPA % (n/N)	95% CI* (%)
Prospectively Collected Specimens	100.0 (134/134)	97.2 - 100.0	90.6 (116/128)**	84.3 - 94.6
Retrospective Specimens	100.0 (30/30)	88.6 - 100.0	96.7 (118/122)**	91.9 - 98.7

*95% Wilson score confidence interval
**Of the 16 discordant samples that were negative by the Final Comparator, 15 samples (11 prospective, 4 retrospective) were reactive by a FDA cleared Treponema pallidum antibody test.

Clinical Performance in Medically Diagnosed Individuals

A total of 151 samples from individuals medically diagnosed with Syphilis were tested in the study. Reactivity of specimens with primary, secondary, and latent syphilis by treatment status is summarized in the table below.

VITROS Syphilis Reactivity in the Medically Diagnosed Population

Syphilis Stage	Treatment Status	N	VITROS Syphilis Results
			Reactive
Primary	Treated	25	25
	Untreated	25	25
Secondary	Treated	25	25
	Untreated	25	25
Latent	Treated	25	25
	Untreated	26	26

Clinical Performance in Apparently Healthy Individuals

A total of 201 prospective specimens from apparently healthy individuals collected from 3 sites in the United States were tested at 3 sites using the VITROS Syphilis test. Reactivity of specimens acquired from apparently healthy individuals is summarized in the table below.

VITROS Syphilis Reactivity in the Apparently Healthy Population

Category	N	VITROS Syphilis Result	
		Reactive N (%)	Non-reactive N (%)
Female	98	2 (2.0)	96 (98.0)
Male	103	2 (1.9)	101 (98.1)
Total	201	4 (2.0)*	197 (98.0)

* Three samples were positive by the Final Comparator.

Expected Values

A total of 924 prospectively collected specimens from the intended use population were tested with the VITROS Syphilis test. The distribution of the VITROS Syphilis reactive and non-reactive results, observed during the clinical study, is summarized below by age and gender. Due to geographic locations or demographics, assay results obtained in individual laboratories may vary from data presented.

Distribution of Reactive and Non-reactive Results Observed in the Clinical Study, by Age and Gender

Age Range (years)	Gender	VITROS Syphilis Results		
		Reactive N (%)	Non-reactive N (%)	Total
18-21	Female	2 (5.7)	33 (94.3)	35
	Male	5 (25.0)	15 (75.0)	20
22-29	Female	5 (3.6)	134 (96.4)	139
	Male	18 (15.7)	97 (84.3)	115
30-39	Female	8 (6.7)	112 (93.3)	120
	Male	77 (41.6)	108 (58.4)	185
40-49	Female	5 (11.6)	38 (88.4)	43
	Male	31 (50.0)	31 (50.0)	62
50-59	Female	5 (16.7)	25 (83.3)	30
	Male	30 (51.7)	28 (48.3)	58
60-69	Female	7 (41.2)	10 (58.8)	17
	Male	33 (45.2)	40 (54.8)	73
≥70	Female	0 (0.0)	4 (100.0)	4
	Male	9 (39.1)	14 (60.9)	23
Combined	Total	235 (25.4)	689 (74.6)	924

Conclusion

The conclusions drawn from the nonclinical and clinical studies (discussed above) demonstrate the VITROS Immunodiagnostic Products Syphilis test is substantially equivalent to the cleared predicate device. The information submitted in the premarket notification is complete and supports a substantial equivalence decision.