May 8, 2024

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

Re: K233581
Trade/Device Name: VITROS Immunodiagnostic Products Total ß-hCG II Reagent Pack
Regulation Number: 21 CFR 862.1155
Regulation Name: Human Chorionic Gonadotropin (HCG) Test System
Regulatory Class: Class II
Product Code: DHA
Dated: March 26, 2024
Received: March 26, 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,

Paula V. Caposino -S

Paula Caposino, Ph.D.
Deputy Director
Division of Chemistry
and Toxicology 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)*
K233581

Device Name
VITROS Immunodiagnostic Products Total β-hCG II Reagent Pack

Indications for Use *(Describe)*
For in vitro diagnostic use only.

For the quantitative measurement of human chorionic gonadotropin (hCG) and its β-subunit in human serum and plasma (heparin and EDTA) using the VITROS 5600 Integrated System to aid in the early detection of pregnancy.

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: K233581.

### Submitter's Information

Ortho Clinical Diagnostics

Felindre Meadows,

Pencoed,

UK CF35 5PZ Phone: +44 (0) 7971 427649

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

### Preparation Date

May 08, 2024

### Device Proprietary Name(s)

VITROS Immunodiagnostic Products Total β-hCG II Reagent Pack

**Common Name(s)** VITROS Total β-hCG II Reagent Pack

### Classification Names

| Product Code | Class | Regulation Section | Panel |
|---|---|---|---|
| DHA | II | 21 CFR 862.1155 | Clinical Chemistry |

### Predicate Device(s)

| Predicate Device | FDA 510(k) Number |
|---|---|
| VITROS Immunodiagnostic Products Total β-hCG II Reagent Pack | K063720 |

### Device Description

The VITROS Immunodiagnostic Products Total β-hCG II Reagent Pack (test) is performed using the VITROS Immunodiagnostic Products Total β-hCG II Reagent Pack and VITROS Immunodiagnostic Products Total β-hCG II Calibrators on the VITROS 5600 Integrated System.

An immunometric immunoassay technique is used, which involves the reaction of human chorionic gonadotropin (hCG) present in the sample with a microwell coated with biotinylated Antibody (mouse monoclonal anti-β-hCG) bound to streptavidin, and a Horseradish Peroxidase (HRP)-labelled antibody conjugate (mouse monoclonal anti-β-hCG). Unbound materials are 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 hCG present in the sample.

VITROS Immunodiagnostic Products Total β-hCG II Reagent Pack contains:

1 reagent pack containing:

- 100 coated wells (antibody, mouse monoclonal anti-β-hCG, binds >600 mIU hCG/well)
- 14.4 mL assay reagent (buffer containing mouse serum, bovine serum albumin, bovine gamma globulin and antimicrobial agent)
- 19.2 mL conjugate reagent (HRP-mouse monoclonal anti-β-hCG, binds ≥4005 mIU hCG/mL) in buffer with bovine serum albumin and antimicrobial agent.

VITROS Total β-hCG II Calibrators contains:

- 3 sets of VITROS Total β-hCG II Calibrators 1, 2 and 3, (freeze-dried, recombinant hCG in human plasma with antimicrobial agent, reconstitution volume 1.0 mL), nominal values 0; 3,000; 14,000 mIU/mL (IU/L)
- 24 calibrator bar code labels (8 for each calibrator)

**Intended Use Statement(s):**
For *in vitro* diagnostic use only.

For the quantitative measurement of human chorionic gonadotropin (hCG) and its β-subunit in human serum and plasma (heparin and EDTA) using the VITROS 5600 Integrated System to aid in the early detection of pregnancy.

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<br>VITROS Immunodiagnostic Products Total β-hCG II reagent pack, K063720, cleared 09 April 2007 | Modified Device<br>VITROS Immunodiagnostic Products Total β-hCG II reagent pack |
|---|---|---|
| Intended Use | For *in vitro* diagnostic use only.<br>For the quantitative measurement of human chorionic gonadotropin (hCG) and its β-subunit in human serum and plasma (heparin and EDTA) using the VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems to aid in the early detection of pregnancy. | For *in vitro* diagnostic use only.<br>For the quantitative measurement of human chorionic gonadotropin (hCG) and its β-subunit in human serum and plasma (heparin and EDTA) using the VITROS 5600 Integrated System to aid in the early detection of pregnancy. |
| Antibody | Mouse Monoclonal anti-β-hCG. | Same. |
| Sample Type | Serum and Plasma. | Same. |
| Sample Volume | 40 µL. | Same. |
| Traceability | Traceable to in-house reference calibrators, which have been value assigned with reference to the 4th International Standard (NIBSC 75/589). | Same. |
| MeasuringRange | Analytical Measuring Interval:<br>2.39– 15,000 mIU/mL (IU/L) | Same. |
| DetectionLimit | LOB: 0.05 mIU/mL (IU/L)<br>LOD: 0.70 mIU/mL (IU/L) | LOB:Same<br>LOD: Same.<br>LOQ: 2.39 mIU/mL (IU/L) |
| Calibrator Levels | 3. | Same. |

## General Device Characteristic Differences:

| | | |
|---|---|---|
| Assay Principle | Sandwich immunoassay | Sandwich immunoassay.<br>In the modified VITROS Immunodiagnostic Products Total β-hCG II reagent pack, the mouse anti-β hCG antibody has been removed from the Biotin Reagent and coated directly onto the well. The modification is to allow the biotinylated antibody capture conjugate to be pre- bound to the well, eliminating the risk of biotin interference. |
| Reagent pack | Biotin-conjugated mouse monoclonal anti-β-hCG coated microwell | Biotin-conjugated mouse monoclonal anti-β-hCG reagent buffer |
| Instrumentation | VITROS 5600 Integrated System | VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems |

## 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 Immunodiagnostic Products Total β-hCG II reagent pack will be 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 a claim of 6 weeks on-board stability currently.

## Precision

Precision was evaluated consistent with CLSI document EP05-A3, *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition*. Six (6) 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 | Units = mIU/mL (IU/L) | | | | | No. of Obs. | No. of Days |
|---|---|---|---|---|---|---|---|
| | Mean hCG Conc. | Repeatability* | | Within Lab** | | | |
| | | SD | %CV | SD | %CV | | |
| 5600 | 5.33 | 0.095 | 1.80% | 0.281 | 5.30% | 80 | 20 |
| | 15.46 | 0.181 | 1.20% | 0.706 | 4.60% | 80 | 20 |
| | 45.67 | 0.666 | 1.50% | 1.560 | 3.40% | 80 | 20 |
| | 297.34 | 4.970 | 1.70% | 8.640 | 2.90% | 80 | 20 |
| | 4708.50 | 82.29 | 1.70% | 151.22 | 3.20% | 80 | 20 |
| | 9651.00 | 286.71 | 3.00% | 464.48 | 4.80% | 80 | 20 |

*Alternate Units (IU/L) are equivalent to Conventional Units (mIU/ml).
**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**

| Sample | Mean | With-in Run | | Between Run | | Within Day | | Between Day | | Between Lot | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | SD | %CV | SD | %CV | SD | %CV | SD | %CV | SD | %CV | SD | %CV |
| PP1 | 5.33 | 0.095 | 1.8% | 0.190 | 3.6% | 0.213 | 4.0% | 0.183 | 3.4% | 0.201 | 3.7% | 0.281 | 5.3% |
| PP2 | 15.46 | 0.181 | 1.2% | 0.647 | 4.2% | 0.672 | 4.3% | 0.215 | 1.4% | 0.706 | 4.4% | 0.706 | 4.6% |
| PP3 | 45.67 | 0.666 | 1.5% | 1.260 | 2.8% | 1.425 | 3.1% | 0.632 | 1.4% | 1.610 | 3.5% | 1.559 | 3.4% |
| PP4 | 297.34 | 4.967 | 1.7% | 4.479 | 1.5% | 6.688 | 2.2% | 5.463 | 1.8% | 12.627 | 4.2% | 8.635 | 2.9% |
| PP5 | 4708.5 | 82.29 | 1.7% | 95.10 | 2.0% | 125.76 | 2.7% | 83.98 | 1.8% | 268.80 | 5.7% | 151.22 | 3.2% |
| PP6 | 9651.0 | 286.71 | 3.0% | 230.87 | 2.4% | 368.11 | 3.8% | 283.26 | 2.9% | 610.09 | 6.4% | 464.48 | 4.8% |

Units = mIU/mL (IU/L)

**Multiple System (Reproducibility) Study Summary**

Six precision fluids (RP1-6) made by pooling female serum samples were evaluated for performance according to CLSI guideline EP05-A3. Five (5) replicates of each fluid were run on one (1) occasion per day for five (5) days The samples were run in randomized order on three (3) VITROS 5600 integrated systems.

| Sample | Mean (mIU/mL) | Within-Run | | Between-Day | | Within-Site | | Between-Site | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | SD | % CV | SD | % CV | SD | % CV | SD | % CV | SD | % CV |
| RP1 | 4.38 | 0.10 | 2.3% | 0.14 | 3.2% | 0.17 | 3.9% | 0.37 | 8.5% | 0.41 | 9.4% |
| RP2 | 15.00 | 0.23 | 1.5% | 0.42 | 2.8% | 0.48 | 3.2% | 0.90 | 6.0% | 1.02 | 6.8% |
| RP3 | 49.55 | 0.77 | 1.6% | 0.94 | 1.9% | 1.21 | 2.5% | 1.96 | 4.0% | 2.31 | 4.7% |
| RP4 | 306.35 | 5.11 | 1.7% | 4.50 | 1.5% | 6.81 | 2.2% | 7.19 | 2.3% | 9.90 | 3.2% |
| RP5 | 4781.1 | 105.94 | 2.2% | 89.54 | 1.9% | 138.70 | 2.9% | 92.27 | 1.9% | 166.59 | 3.5% |
| RP6 | 8329.9 | 249.62 | 3.0% | 219.68 | 2.6% | 332.52 | 4.0% | 220.88 | 2.7% | 399.20 | 4.8% |

## Detection Capability

Detection studies for the VITROS Immunodiagnostic Products Total β-hCG II reagent pack were evaluated consistent with CLSI document EP17-A2, *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline* – Second Edition. Four serums containing no measurable human chorionic gonadotropin (hCG) 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. The representative LoB is 0.00 mIU/mL (IU/L) which supports the claimed LOB of 0.05mIU/mL.

Five samples were used for establishing the LoD, which were targeted at 1 to 5 times the LoB concentration. The LoD samples were neat serum samples containing low levels of endogenous hCG to achieve the approximate target hCG concentrations. The LoD serums were also used to analyze the LoQ via the Precision Profile method. The Total Error Analysis for LoQ was determined by testing a separate set of four LoQ fluids which were then analyzed to calculate the LoQ via the Total Error method. 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 representative Limit of Detection (LoD) for the VITROS Immunodiagnostic Products Total β-hCG II reagent pack is 0.21 mIU/mL (IU/L) determined consistent with CLSI document EP17. This supports the claimed LoD of 0.70 mIU/mL (IU/L). The Limit of Quantitation (LoQ) for the VITROS Immunodiagnostic Products Total β-hCG II reagent pack was designed to be less than or equal to the currently claimed low end of the measuring range of 2.39 mIU/mL (IU/L) at 20% CV. The representative LoQ using the Total Error approach was determined to be 2.32 mIU/mL (IU/L), consistent with CLSI document EP17. The claimed LoQ has been verified at 2.39 mIU/mL (IU/L).

**Linearity**

Linearity was established in accordance with the CLSI guideline EP06 2nd edition. In a study with two series, one across the entire range (pools 1a to 10a) and one in the lower range of the assay (pools 1b to 10b). 10 replicates of pools 1a/1b and 10a/10b, and 5 replicates of pools 2a/2b to 9a/9b were run on one VITROS 5600 Integrated System. Results support linearity from 1.51 mIU/mL (IU/L) to 15695 mIU/mL (IU/L).

| | | | Slope | | Intercept | | |
|---|---|---|---|---|---|---|---|
| **Lot** | **Dilution Range** | **% Recovery** | **Estimate** | **95% CI** | **Estimate** | **95% CI** | **$R^2$** |
| 2643 | 38.6 to 15695 | 92.2% to 108.2% | 0.991 | 0.949 to 1.033 | 0.10 | -2.56 to 2.76 | 0.996 |
| 2643 | 1.51 to 51.18 | 99.9% to 112.7% | 1.025 | 0.995 to 1.056 | 0.07 | -0.09 to 0.22 | 0.999 |

**Measuring Range**

| VITROS System | Measuring (Reportable) Range |
|---|---|
| 5600 | 2.39*–15,000 mIU/mL(IU/L) |

* Lower limit of measuring range reported by the system software is based on the Limit of Quantitation.

**Matrix Comparison**

Serum and plasma (Lithium-Heparin and K2-EDTA) specimen matrices were determined to be equivalent. The results met the acceptance criteria for the comparison between serum and plasma (Lithium-Heparin and K2-EDTA) specimens spanning the expected measuring interval. Based on the analysis, serum and plasma (Lithium-Heparin and K2-EDTA) are suitable specimen matrices for use with the VITROS Immunodiagnostic Products Total β-hCG II reagent pack.

Specimens Recommended

- Serum
- Lithium-HeparinPlasma
- K2- EDTA Plasma

Specimens Not Recommended

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

| VITROS 5600 | | |
|---|---|---|
| Weighted Deming Regression | Li-Hep Plasma | K2-EDTA Plasma |
| Slope | 0.978 | 0.978 |
| Corr. Coef r | 0.999 | 0.999 |
| n | 41 | 41 |

**Analytical Specificity**

**Known Interferents**
The VITROS Immunodiagnostic Products Total β-hCG II reagent pack was screened for interfering substances at hCG concentrations of approximately 5.00 mIU/mL (IU/L), 50.00 mIU/mL (IU/L), and 10,000 mIU/mL (IU/L) following CLSI EP07 and EP37. Of the compounds tested, none was found to cause a 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 Immunodiagnostic Products Total β-Hcg II reagent pack following CLSI EP07and EP37 and found not to cause bias > 10% at Hcg concentrations of approximately 5.00 mIU/mL (IU/L), 50.00 mIU/mL (IU/L), and 10,000 mIU/mL (IU/L) at the test concentrations shown.

| Substance | Concentration | |
|---|---|---|
| Acetaminophen | 15.6 mg/Dl | 1032 µmol/L |
| N-Acetylcysteine | 15.0 mg/Dl | 920 µmol/L |
| Alpha-tocopherol | 6.45 mg/Dl | 150 µmol/L |
| Amoxicillin | 5.40 mg/Dl | 148 µmol/L |
| Ascorbic acid | 5.25 mg/Dl | 298 µmol/L |
| Bilirubin, conjugated | 40 mg/Dl | 475 µmol/L |
| Bilirubin, unconjugated | 40 mg/Dl | 475 µmol/L |
| Biotin | 0.351 mg/Dl | 14.3 µmol/L |
| Carbamazepine | 4.50 mg/Dl | 191 µmol/L |
| Cefoxitin sodium | 695 mg/Dl | 15.5 mmol/L |
| Cholesterol | 400 mg/Dl | 10.3 mmol/L |
| Codeine | 0.141 mg/Dl | 5 µmol/L |
| Colecalciferol | 19.2 µg/Dl | 0.5 µmol/L |
| Cotinine | 0.24 mg/Dl | 13.6 µmol/L |
| Dextran 40 | 2400 mg/Dl | 600 µmol/L |
| Dextromethorphan | 0.00156 mg/Dl | 0.042 µmol/L |
| Dipyrone | 100 mg/Dl | N/A |
| Enoxaparin | 360 U/Dl | N/A |
| Ethanol | 600 mg/Dl | 130 mmol/L |

| Substance | Concentration | |
|---|---|---|
| Furosemide | 1.59 mg/Dl | 48 µmol/L |
| Gamma globulin | 6 g/Dl | N/A |
| HAMA (Human Anti-Mouse Antibodies) | 800 µg/L | 0.005 µmol/L |
| Hemoglobin | 1000 mg/Dl | 155 µmol/L |
| Hydralazine hydrochloride | 1.44 mg/Dl | 73.2 µmol/L |
| Hydrocodone | 0.0072 mg/Dl | 0.2 µmol/L |
| Ibuprofen | 21.9 mg/Dl | 1.06 mmol/L |
| Intralipid | 2000 mg/Dl | 19.2 mmol/L |
| Levothyroxine | 0.0429 mg/Dl | 0.552 µmol/L |
| Loratadine | 0.0087 mg/Dl | 0.227 µmol/L |
| Naproxen | 36.0 mg/Dl | 1.43 mmol/L |
| Nifedipine | 0.0588 mg/Dl | 1.7 µmol/L |
| Nitrofurantoin | 0.213 mg/Dl | 8.94 µmol/L |
| Omeprazole | 0.840 mg/Dl | 24.3 µmol/L |
| Phenytoin | 6.00 mg/Dl | 238 µmol/L |
| Prednisone | 0.010 mg/Dl | 0.280 µmol/L |
| Propranolol HCl | 0.115 mg/Dl | 3.89 µmol/L |
| Rheumatoid factor | 900 IU/Ml | N/A |
| Salicylic acid | 2.86 mg/Dl | 207 mmol/L |
| Sodium azide | 100 mg/Dl | 15.4 mmol/L |
| Sulfamethoxazole | 40 mg/Dl | 1.58 mmol/L |
| Theophylline | 6.0 mg/Dl | 333 µmol/L |
| Total Protein | 15 g/Dl | 17.1 nmol/L |
| Triglycerides | 1500 mg/Dl | 16.9 mmol/L |
| Trimethoprim | 4.2 mg/Dl | 145 µmol/L |
| Vancomycin hydrochloride | 12.3 mg/Dl | 8.28 mmol/L |

**Cross-Reactivity**

The cross-reactivity of the VITROS Immunodiagnostic Products Total β-hCG II reagent pack was evaluated by adding the following test substances to a sample containing no hCG.

% Cross-Reactivity Summary with a hCG Negative Sample

| Substance | Tested Concentration | VITROS 5600 - % Cross Reactivity |
|---|---|---|
| FSH | 400 mIU/mL | ND |
| LH | 400 mIU/mL | ND |
| TSH | 200 mIU/mL | ND |

*Not Detectable (ND). Concentration was below the measuring interval of the test, 2.39 to 15,000 mIU/mL (IU/L).

Each potential cross-reactant was spiked into hCG pools at hCG concentrations of approximately 25 mIU/mL Test substances were spiked at a volume that constituted no more than 5% of the volume of the test sample.

% Cross-Reactivity Summary with a Pool at hCG Concentrations of Approximately 25 mIU/mL.

| Substance | Tested Concentration | % Cross Reactivity |
|---|---|---|
| FSH | 400 mIU/mL | 0.6% |
| LH | 400 mIU/mL | -0.3% |
| TSH | 200 mIU/mL | 0.4% |

**Dilution**

Samples with concentrations greater than the measuring range may be diluted automatically on the system up to 400-fold (1 part sample with 399 parts diluent) by the VITROS Integrated System with VITROS High Sample Diluent B Reagent Pack prior to test. Refer to the 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 hCG values from 180 normal healthy non-pregnant blood donors showed equivalency to the expected values claim published in the Instructions for Use of the current VITROS Immunodiagnostic Products Total β-hCG II Reagent Pack, therefore the current distribution of results for healthy non-pregnant subjects will be transferred to the updated VITROS Immunodiagnostic Products Total β-hCG II Reagent Pack.

Product Claim:

| Sample type | Number of samples | Units = mIU/mL (IU/L) | | | | |
|---|---|---|---|---|---|---|
| | | Mean | Min | Max | 2.5th Percentile | 97.5th Percentile |
| Normal Male | 98 | 0.02 | 0.00 | 1.06 | 0.00 | 0.08 |
| Normal Female | 123 | 0.46 | 0.00 | 5.42 | 0.00 | 4.32 |
| Post menopausal | 69 | 1.52 | 0.00 | 6.66 | 0.00 | 6.46 |
| Total | 290 | 0.56 | 0.00 | 6.66 | 0.00 | 4.83 |

- As a guide, the following ranges were determined. Concentrations of hCG measured in samples from apparently healthy, non-

pregnant individuals were determined to be ≤4.83 mIU/mL (IU/L) (290 samples).

Distribution of Healthy Subjects Results for the updated VITROS Immunodiagnostic Products Total β-hCG II reagent pack:

| Sample Type | Number of Samples | Units (mIU/mL) | | | | |
|---|---|---|---|---|---|---|
| | | Mean | Min | Max | 2.5th Percentile | 97.5th Percentile |
| Normal Male | 60 | 0.00 | 0.00 | 0.04 | 0.00 | 0.04 |
| Normal Female | 60 | 0.07 | 0.00 | 2.78 | 0.00 | 1.44 |
| Post-Menopausal | 60 | 1.32 | 0.00 | 5.61 | 0.00 | 5.08 |
| Total | 180 | 0.47 | 0.00 | 5.61 | 0.00 | 3.73 |

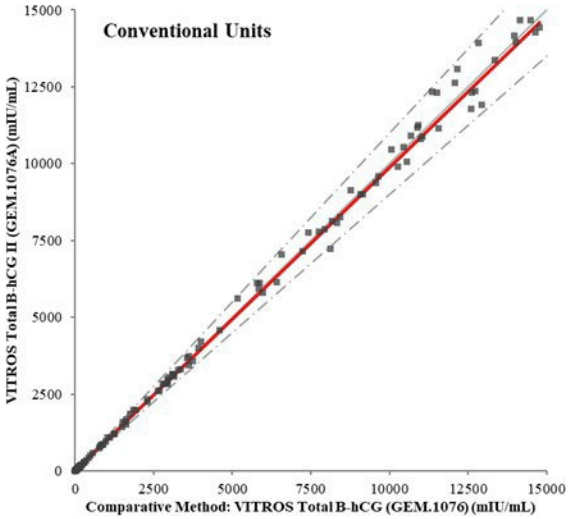
**Traceability of Calibration**

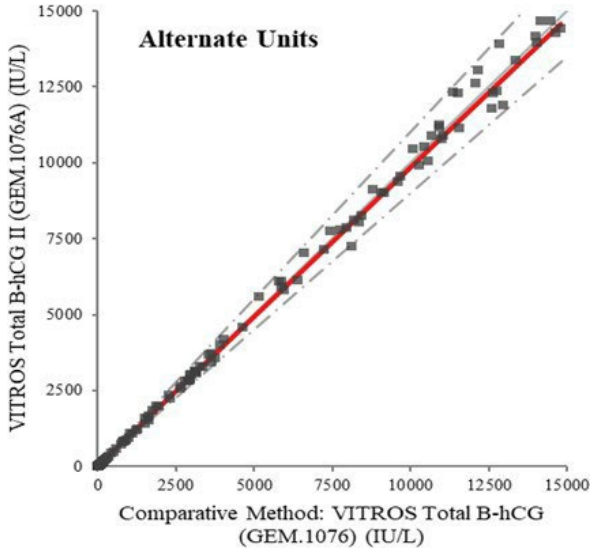
Calibration of the VITROS Immunodiagnostic Products Total β-hCG II reagent pack is traceable to in-house reference calibrators, which have been value-assigned with reference to the 4th International Standard (NIBSC 75/589).

**Method Comparison**

Accuracy was evaluated consistent with CLSI guideline EP09c *Measurement Procedure Comparison and Bias Estimation Using Patient Samples. 3rd ed.* Human serum samples were obtained from certified vendors and tested neat. A total of 135 samples analyzed. The samples were tested in singleton using one reagent lot and one VITROS 5600 Integrated System.

The plots and table show the results of a method comparison study using patient serum samples analyzed on the VITROS Immunodiagnostic Products Total β-hCG II reagent pack compared with those analyzed on the VITROS Immunodiagnostic Products Total β-hCG II reagent pack (GEM.1076) on the VITROS 5600 Integrated System. The relationship between the 2 methods was determined by Weighted Deming regression.



| System | *n* | Slope (95% CI) | Correlation Coefficient | Conventional Units (mIU/mL) | | Alternate Units (IU/L) | |
|---|---|---|---|---|---|---|---|
| | | | | Range of Samples | Intercept (95% CI) | Range of Samples | Intercept (95% CI) |
| 5600 vs. Comparative Method | 135 | 0.99 (0.977 to 0.995) | 0.998 | 2.78-14,675 | -0.0215 (-0.160 to 0.117) | 2.78-14,675 | -0.0215 (-0.160 to 0.117) |

**Conclusion**

The conclusions drawn from the nonclinical tests (discussed above) demonstrate the updated VITROS Immunodiagnostic Products Total β-hCG II 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.