VITROS Products Immunodiagnostic

INSTRUCTIONS FOR USE E2

VITROS Immunodiagnostic Products Estradiol Reagent Pack	REF	855 2630
VITROS Immunodiagnostic Products Estradiol Calibrators	REF	131 8930

Rx ONLY

Intended Use

For *in vitro* diagnostic use only.

VITROS Immunodiagnostic Products Estradiol Reagent Pack

For the quantitative measurement of estradiol in human serum and plasma (heparin or EDTA) using the VITROS ECi/ECiQ/ 3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems.

VITROS Immunodiagnostic Products Estradiol Calibrators

For use in the calibration of the VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems for the quantitative measurement of estradiol in human serum and plasma (heparin or EDTA).

Summary and Explanation of the Test

Estradiol is produced by the adrenals, placenta, and testes and is the principal estrogen secreted by the ovaries. Over 98% of circulating estradiol is bound to serum proteins, principally sex hormone binding globulin (SHBG). Metabolic clearance of estradiol is effected by conversion to estrone, and by hydroxylation and conjugation with sulfate or glucuronide. [1-3] Estradiol normally exerts negative feedback control on gonadotropin release, however, as estradiol production accelerates with the rapid growth of the dominant follicle, this feedback becomes positive, causing a surge in LH secretion, and ovulation occurs. [4] The measurement of estradiol is useful in assessing a variety of menstrual dysfunctions including delayed puberty, amenorrhoea and menopause.

Principles of the Procedure

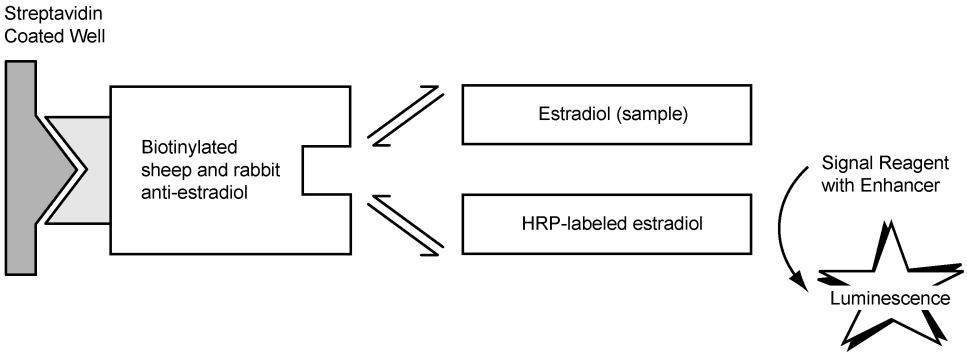
A competitive immunoassay technique is used, which depends on a competition between estradiol present in the sample with a horseradish peroxidase (HRP)-labeled estradiol conjugate for a limited number of binding sites on a mixture of biotinylated antibodies (sheep and rabbit anti-estradiol). The antigen-antibody complex is captured by streptavidin on the wells. Unbound materials are removed by washing.

The bound HRP conjugate is measured by a luminescent reaction. [5] 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 indirectly proportional to the concentration of estradiol present.

Test Type	System *	Incubation Time	Time to first result	Test Temperature	Reaction Sample Volume
Competitive immunoassay	ECi/ECiQ, 3600, 5600, XT 7600	32 minutes	40 minutes	37 °C	25 µL

* Not all products and systems are available in all countries.

Reaction Scheme



Warnings and Precautions

WARNING:	*Potentially Infectious Material* *Human blood products provided as components of the VITROS Estradiol Reagent Pack and the VITROS Estradiol Calibrators have been obtained from donors who were tested individually and who were found to be negative for hepatitis B surface antigen, and for antibodies to human immunodeficiency virus (HIV 1+2) and hepatitis C virus (HCV), using approved methods (enzyme immunoassays). Treat as if capable of transmitting infection.* *Use caution when handling material of human origin. Consider all samples potentially infectious. No test method can offer complete assurance that hepatitis B virus, HCV, HIV 1+2 or other infectious agents are absent. Handle, use, store and dispose of solid and liquid waste from samples and test components, in accordance with procedures defined by appropriate national biohazard safety guideline or regulation (e.g. CLSI document M29).* [6]
WARNING:	*Contains Kathon or ProClin 200 (CAS 55965-84-9)* [7] *The VITROS Estradiol Reagent Pack and VITROS Estradiol Calibrators contain 0.5% and 2.0% Kathon or ProClin 200 respectively. H317: May cause an allergic skin reaction. H319: Causes serious eye irritation. P280: Wear protective gloves, Eye Protection. P302 + P352: IF ON SKIN: Wash with plenty of soap and water. P305 + P351 + P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P333 + P313: If skin irritation or rash occurs: Get medical advice/attention. P337 + P313: If eye irritation persists: Get medical advice/attention. P362: Take off contaminated clothing and wash before reuse.* *Refer to www.Orthoclinicaldiagnostics.com for the Safety Data Sheets and for Ortho contact information.*

WARNING

Reagents

Reagent Pack Contents

1 reagent pack containing:

- 100 coated wells (streptavidin, bacterial, binds ≥2 ng biotin/well)
- 13.3 mL conjugate reagent (HRP-estradiol, ≥80 ng/mL) in buffer with bovine serum albumin and antimicrobial agent

- 8.4 mL biotinylated antibody reagent (biotin-rabbit anti-estradiol and biotin-sheep anti-estradiol, binds ≥7 pmol estradiol/mL) in buffer with human serum and antimicrobial agent

Reagent Pack Handling

- The reagent pack is supplied ready for use.
- The reagent pack contains homogeneous liquid reagents that do not require shaking or mixing prior to loading on the system.
- As with all immunoassay protein-based solutions, inappropriate handling of the reagent pack can cause foam to occur on the surface of the reagent. Avoid agitation, which may cause foaming or the formation of bubbles.
  - If reagent packs are dropped or agitated, small levels of fine foam could be generated that may not be detected by the system.
  - Reagent packs containing fine foam that is not detected by the system, may show a positive bias.
- If you must use a dropped or agitated reagent pack before it has been allowed to settle, you should verify performance by running high and low quality control samples in duplicate after loading the pack on the system.

Reagent Pack Storage and Preparation

Reagent	Storage Condition		Stability
Unopened	Refrigerated	2–8 °C (36–46 °F)	expiration date
Opened	On system	System turned on	≤8 weeks
Opened	Refrigerated	2–8 °C (36–46 °F)	≤8 weeks

- The VITROS Estradiol Reagent Pack is suitable for use until the expiration date on the carton when stored and handled as specified. Do not use beyond the expiration date.
- Do not freeze unopened reagent packs.
- Load reagent packs directly from refrigerated storage to minimize condensation.
- Store opened refrigerated reagent packs in a sealed reagent pack storage box that contains dry desiccant.

Calibrator Contents

- 1 set of VITROS Estradiol Calibrators 1 and 2 (estradiol in human serum, with antimicrobial agent, 2 mL); nominal values 150 and 5000 pmol/L (40.9 and 1362 pg/mL)
- Lot calibration card
- Protocol card
- 16 calibrator bar code labels (8 for each calibrator)

Calibrator Handling

- Use only with reagent packs of the same lot number. Mix thoroughly by inversion and bring to 15–30 °C (59–86 °F) before use. Each pack contains sufficient for a minimum of 6 determinations of each calibrator.
- Handle calibrators in stoppered containers to avoid contamination and evaporation. To avoid evaporation, limit the amount of time calibrators are on the system. Refer to the operating instructions for your system. Return to 2–8 °C (36–46 °F) as soon as possible after use, or load only sufficient for a single determination.

Calibrator Storage and Preparation

Calibrator	Storage Condition		Stability
Unopened	Refrigerated	2–8 °C (36–46 °F)	expiration date
Opened	Refrigerated	2–8 °C (36–46 °F)	≤13 weeks
Opened	Frozen	≤-20 °C (≤-4 °F)	≤13 weeks

- VITROS Estradiol Calibrators are supplied ready for use.
- VITROS Estradiol Calibrators are suitable for use until the expiration date on the carton when stored and handled as specified. Do not use beyond the expiration date.
- Opened calibrators may be stored frozen (with no more than 1 freeze-thaw cycle).
- The VITROS Estradiol test uses 25 µL of calibrator for each determination. The VITROS Estradiol Calibrators may be used directly on the VITROS Immunodiagnostic and VITROS Integrated Systems. Alternatively, transfer an aliquot of each calibrator into a sample container (taking account of the minimum fill volume of the container), which may be bar coded with the labels provided. For details on minimum fill volume of sample cups or containers, refer to the operating instructions for your system.

Specimen Collection, Preparation and Storage

Patient Preparation

No special patient preparation is necessary.

Specimens Recommended

- Serum
- Heparin plasma
- EDTA plasma

Specimens Not Recommended

- Do not use turbid specimens. Turbidity in specimens may affect test results.
- Do not use hemolysed samples as hemolysis may affect test results.

Special Precautions

IMPORTANT:	*Certain collection devices have been reported to affect other analytes and tests.*[8] *Owing to the variety of specimen collection devices available, Ortho Clinical Diagnostics is unable to provide a definitive statement on the performance of its products with these devices. Confirm that your collection devices are compatible with this test.*

Specimen Collection and Preparation

- Collect specimens using standard procedures.[9-10]
- Thoroughly mix samples by inversion and bring to 15–30 °C (59–86 °F) before use.
- The VITROS Estradiol test uses 25 µL of sample for each determination. This does not take account of the minimum fill volume of the chosen sample container. For details on minimum fill volume of sample cups or containers, refer to the operating instructions for your system.

Handling and Storage Conditions

- Handle samples in stoppered containers to avoid contamination and evaporation.
- The amount of time samples are on the system prior to analysis should be limited to avoid evaporation. Refer to the operating instructions for your system for further information.
- Return to 2–8 °C (36–46 °F) as soon as possible after use, or load sufficient volume for a single determination.
- Serum and plasma samples may be stored for up to 2 days at 2–8 °C (36–46 °F) or 4 weeks at -20 °C (-4 °F).
- Avoid repeated freeze-thaw cycles.

Testing Procedure

Materials Provided

- VITROS Immunodiagnostic Products Estradiol Reagent Pack
- VITROS Immunodiagnostic Products Estradiol Calibrators

Materials Required but Not Provided

The following items are required to perform the VITROS Estradiol test:

- VITROS Immunodiagnostic Products Signal Reagent
- VITROS Immunodiagnostic Products Universal Wash Reagent
- VITROS Immunodiagnostic Products High Sample Diluent A Reagent Pack
- Quality control materials such as the VITROS Immunodiagnostic Products RE Controls
- VITROS Immunodiagnostic Products Reagent Pack Storage Box (optional) with desiccant

Operating Instructions

Check the inventory regularly to aid the management of reagents and ensure that sufficient VITROS Signal Reagent, VITROS Universal Wash Reagent and calibrated reagent lots are available for the work planned. When performing panels of tests on a single sample, ensure that the sample volume is sufficient for the tests ordered.

For detailed information refer to the operating instructions for your system.

Note:	Do not use visibly damaged product.

Sample Dilution

Serum samples with concentrations greater than the measuring range may be automatically diluted on the system up to 5-fold (1 part sample with 4 parts diluent) by the VITROS Immunodiagnostic and VITROS Integrated Systems with the VITROS High Sample Diluent A Reagent Pack prior to test. Refer to the VITROS High Sample Diluent A Reagent Pack instructions for use.

Default Test Name

The default test name which will appear on patient reports is Estradiol. The default short name that will appear on the test selection menus and laboratory reports is E2. These defaults may be reconfigured, if required. For detailed information refer to the operating instructions for your system.

Calibration

Calibration Procedure

- Calibration is lot specific; reagent packs and calibrators are linked by lot number. Reagent packs from the same lot may use the same calibration.
- A Master Calibration (a dose response curve covering the full calibration range) is established for each new reagent lot. Concentrations for the linked lot of calibrators are determined from the Master Calibration.
- Ensure that the Master Calibration for each new reagent lot is available on your system.
- Process calibrators in the same manner as samples. Calibration need not be programmed if bar code labels are used; load the calibrators in any order, calibration will be initiated automatically.
- When the calibrators are processed the signal expected for each calibrator is compared against the actual signal obtained. The Master Calibration is then rescaled to reflect the differences between the actual and expected signals. The validity of this calibration curve is assessed against a range of quality parameters, and if acceptable, it is stored for use with any reagent pack of that lot.
- The quality of calibration cannot be completely described by a single parameter. The calibration report should be used in conjunction with acceptable control values to determine the validity of the calibration.
- Recalibration is required after a pre-determined calibration interval, or when a different reagent lot is loaded.
- Calibration results are assessed against a range of quality parameters. Failure to meet any of the defined quality parameter ranges will be coded in the calibration report. For actions to be taken following a failed calibration refer to the operating instructions for your system.

Refer to the operating instructions for your system for detailed instructions on the calibration process.

When to Calibrate

- Calibrate when the reagent pack and calibrator lot changes.
- Calibrate every 28 days.
- After specified service procedures have been performed.
- If quality control results are consistently outside of your acceptable range.

For additional information on when to calibrate, refer to the operating instructions for your system.

Traceability of Calibration

Calibration of the VITROS Estradiol test is traceable to in-house reference calibrators, which have been value-assigned to correlate to samples measured by isotope dilution-gas-chromatography/mass spectrometry (ID-GC/MS).

Calibration Model

A modified four-parameter logistic curve fit function is used to construct the Master Calibration. The calibration process rescales the Master Calibration to establish a valid stored curve for the VITROS Immunodiagnostic and VITROS Integrated Systems.

Measuring (Reportable) Range

System	Measuring (Reportable) Range
3600 5600 XT 7600 ECi/ECiQ	23.347*–14,000 pmol/L (6.360–3813.6 pg/mL)

* Lower Limit of measuring range reported by the system software is based on the Limit of Detection

The lower limit reported by the system can be reconfigured if desired. For details on how to reconfigure the lower limit refer to the operating instructions for your system.

Quality Control

Quality Control Material Selection

VITROS RE Controls are recommended for use with the VITROS Immunodiagnostic and VITROS Integrated Systems. The VITROS RE Controls contain 3 levels of estradiol (low, medium and high). The performance of other commercial control fluids should be evaluated for compatibility with this test before they are used for quality control.

Control materials may show a difference when compared with other estradiol methods if they contain high concentrations of preservatives, stabilizers, or other nonphysiological additives, or otherwise depart from a true human sample matrix.

Appropriate quality control value ranges must be established for all quality control materials used with the VITROS Estradiol test.

Quality Control Procedure Recommendations

- Good laboratory practice requires that controls be processed to verify the performance of the test.
- Choose control levels that check the clinically relevant concentrations.
- To verify system performance, analyze control materials:
  - After calibration
  - According to local regulations or at least once each day that the test is being performed
  - After specified service procedures are performed

If quality control procedures within your laboratory require more frequent use of controls, follow those procedures.

- Analyze quality control materials in the same manner as patient specimens.
- If control results fall outside your acceptable range, investigate the cause before deciding whether to report patient results.
- Refer to published guidelines for general quality control recommendations. [11]

For more detailed information, refer to the operating instructions for your system.

Quality Control Material Preparation and Storage

Refer to the manufacturer's product literature for preparation, storage, and stability information.

Results

Results are automatically calculated by the VITROS Immunodiagnostic and VITROS Integrated Systems.

Reporting Units and Unit Conversion

Analyte results are quoted in units of pmol/L or pg/mL. To configure the units, refer to the operating instructions for your system.

Conventional	Alternate
pmol/L (pg/mL× 3.67)	pg/mL (pmol/L× 0.2724)

Limitations of the Procedure

WARNING: ***Drugs of estradiol derivatives can interfere with estradiol measurement by immunoassay, resulting in falsely elevated estradiol results.***

Known Interferences

The VITROS Estradiol test was evaluated for interference consistent with CLSI document EP7. [12] Commonly encountered substances were tested on 2 lots of reagents. The following compounds when tested caused the bias shown at the concentrations indicated.

Refer to "Specificity" for a list of other compounds tested that did not show interference.

Interferent	Interferent Concentration		Units = pmol/L		Units = pg/mL	
			Analyte Conc.*	Bias**	Analyte Conc.*	Bias**
Bilirubin***	0.342 mmol/L	20 mg/dL	2750	476	749	130
Hemoglobin****	0.31 mmol/L	500 mg/dL	1583	-203	431	-55.3

* Average test concentration of replicate determinations using 2 different lots of reagent.

** Estimate of the average difference observed.

*** Bilirubin data derived from one Master Kit Lot.

**** Hemolysate was added to a series of specimens with VITROS Estradiol concentrations of 116–4098 pmol/L (31.6-1116.3 pg/mL)

Note: These results are representative. The degree of interference at concentrations other than those listed might not be predictable from these results. Other interfering substances may be encountered in the patient population.

Other Limitations

- The results from this or any other diagnostic test should be used and interpreted only in the context of the overall clinical picture.
- Heterophilic antibodies in serum or plasma samples may cause interference in immunoassays. [13] 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.
- Inaccurate results may be caused by steroid therapy or physiological conditions causing large changes in serum protein concentrations. Elevated estradiol concentrations may be due to defects in steroid metabolism remote from the hypothalamic-pituitary-gonadal axis.
- Certain drugs and clinical conditions are known to alter estradiol concentrations in vivo. Please consult one of the published summaries for details. [14- 16]
- Biotin levels in serum remain elevated for up to 24 hours after oral or intravenous biotin administration. [17]

Expected Values and Interpretation of Results

It is recommended that each laboratory establish its own expected values for the population it serves.

Reference Interval

Phase	No. of Samples	Units = pmol/L	Units = pg/mL
Normal female follicular	59	97.5–592	26.6–161
Normal pre-ovulatory peak	15	685–1404	187–382
Normal female luteal	156	120–738	32.7–201
Postmenopausal females	46	19.7–141	5.37–38.4
Normal males	46	19.7–242	5.37–65.9

These reference intervals are the central 95% of results from studies of:

- female patients during the normal follicular phase, pre-ovulatory peak, and normal luteal phase, determined from 15 normal menstrual cycles
- postmenopausal females
- normal males

Interpretation of Results

For patient sample values outside of your established reference interval, the system may be configured to display a flag ‘LO’ or ‘HI’. Refer to the operating instructions for your system.

Performance Characteristics

Limit of Detection

The Limit of Detection (LoD) for VITROS Estradiol is 23.347 pmol/L (6.360 pg/mL), determined consistent with NCCLS document EP17 [18] and with proportions of false positives (α) less than 5% and false negatives (β) less than 1%; based on 693 determinations, with 1 blank and 5 low-level samples. The Limit of Blank (LoB) is 8.029 pmol/L (2.187 pg/mL).

Limit of Blank and Limit of Detection

LoB*		LoD**	
pmol/L	pg/mL	pmol/L	pg/mL
8.029	2.187	23.347	6.360

* Limit of Blank, or the highest value likely to be observed with a sample containing no analyte, replaces the term "analytical sensitivity."

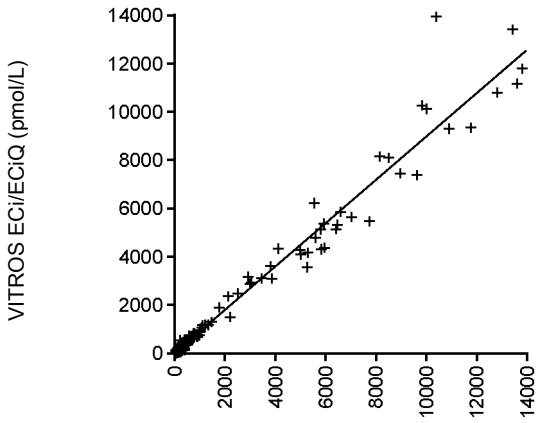
** Proportions of false positives (α) and false negatives (β) were less than 5% and 1% respectively; based on 693 determinations, with 1 blank and 5 low-level samples.

Accuracy (Method Comparison)

Accuracy was evaluated consistent with NCCLS document EP9. [19] The plots and table show the results of a method comparison study using patient samples from a variety of clinical categories analyzed on the VITROS ECi/ECiQ Immunodiagnostic System compared with those analyzed using the *Amerlite* Estradiol-60 test. The relationship between the 2 methods was determined by Deming regression. [20]

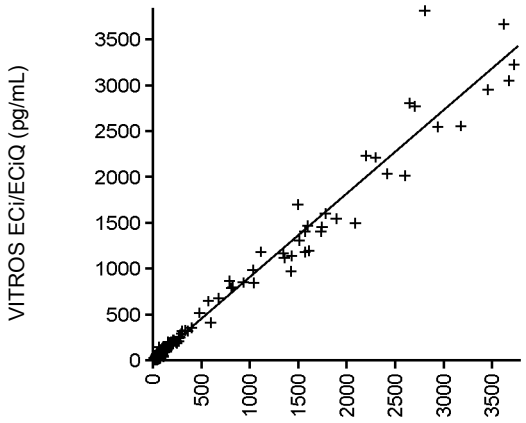
The table also shows the results of method comparison studies [21] using patient serum and plasma samples analyzed on the VITROS ECi/ECiQ Immunodiagnostic System compared with those analyzed using the VITROS 3600 Immunodiagnostic System and the VITROS 5600 Integrated System. The relationship between the 2 methods was determined by Deming regression. [20]

Conventional Units



Comparative Method:
Amerlite Estradiol-60 test (pmol/L)

Alternate Units



Comparative Method:
Amerlite Estradiol-60 test (pg/mL)

System	n	Slope	Correlation Coefficient	Conventional Units (pmol/L) Range of Samples	Conventional Units (pmol/L) Intercept	Alternate Units (pg/mL) Range of Samples	Alternate Units (pg/mL) Intercept
ECi/ECiQ vs. Comparative Method	199	0.909	0.985	16.9–13,971	-22.3	4.60–3806	-6.07
3600 vs. ECi/ECiQ	103	1.00	0.991	54.8–13,489	-7.87	14.9–3674	-2.14
5600* vs. ECi/ECiQ	102	1.07	0.993	54.8–12,008	-12.2	14.9–3271	-3.32

* Performance characteristics for the VITROS 5600 System are applicable to the VITROS XT 7600 System.

Precision

VITROS ECi/ECiQ Immunodiagnostic System

Precision was evaluated consistent with NCCLS document EP5. [22] One replicate of the first level freeze-dried control and 2 replicates each of the remaining 3 freeze-dried control samples were tested on 2 separate occasions per day on at least 20 different days. The experiment was performed using 2 reagent lots on 2 different systems. The data presented are a representation of the product performance.

VITROS 3600 Immunodiagnostic System and VITROS 5600 Integrated System

Precision was evaluated consistent with NCCLS document EP5. [23] Two replicates of each of 3 freeze-dried control samples were tested on 2 separate occasions per day on at least 20 different days. The experiment was performed using 1 reagent lot on each system. The data presented are a representation of the product performance.

System	Units = pmol/L							No. Observ.	No. Days
	Mean Estradiol Conc.	Within-run*		Within-calibration**		Within-lab***			
		SD	CV (%)	SD	CV (%)	SD	CV (%)		
ECi/ECiQ system 1	201	13.3	6.6	14.8	7.4	17.7	8.8	42	21
	241	8.90	3.7	18.6	7.7	22.3	9.3	84	21
	1356	25.3	1.9	53.3	3.9	70.8	5.2	84	21
	4711	59.7	1.3	136	2.9	225	4.8	84	21
ECi/ECiQ system 2	206	8.65	4.2	11.8	5.7	13.5	6.6	40	20
	270	8.78	3.3	17.8	6.6	19.3	7.1	80	20
	1359	21.1	1.6	65.6	4.8	57.2	4.2	79	20
	4691	63.3	1.3	165	3.5	158	3.4	80	20
3600	186	6.65	3.5	10.3	5.5	11.6	6.0	92	23
	1235	22.0	1.8	35.1	2.8	44.5	3.5	92	23
	5691	109	1.9	131	2.3	183	3.2	92	23
5600****	197	5.58	2.8	18.8	9.5	21.9	11.5	88	22
	1284	18.4	1.4	68.7	5.4	81.8	6.6	88	22
	5999	61.3	1.0	219	3.6	271	4.7	88	22

* Within-run (repeatability). Between Duplicate precision averaged over all runs

** Within-calibration. Total precision with weighted components of within-run, between–run and between-day variation

*** Within-lab. A measure of the effect of recalibration on total precision, calculated within reagent lot, using data from at least 4 calibrations

**** Performance characteristics for the VITROS 5600 System are applicable to the VITROS XT 7600 System.

System	Units = pg/mL							No. Observ.	No. Days
	Mean Estradiol Conc.	Within-run*		Within-calibration**		Within-lab***			
		SD	CV (%)	SD	CV (%)	SD	CV (%)		
ECi/ECiQ system 1	54.8	3.62	6.6	4.03	7.4	4.82	8.8	42	21
	65.6	2.42	3.7	5.07	7.7	6.07	9.3	84	21
	369	6.89	1.9	14.5	3.9	19.3	5.2	84	21
	1283	16.3	1.3	37.0	2.9	61.3	4.8	84	21
ECi/ECiQ system 2	56.1	2.36	4.2	3.21	5.7	3.68	6.6	40	20
	73.5	2.39	3.3	4.85	6.6	5.26	7.2	80	20
	370	5.75	1.6	17.9	4.8	15.6	4.2	79	20
	1278	17.2	1.3	44.9	3.5	43.0	3.4	80	20
3600	50.7	1.80	3.5	2.81	5.5	3.16	6.2	92	23
	336	5.99	1.8	9.56	2.9	12.1	3.5	92	23
	1550	29.7	1.9	35.7	2.3	50.0	3.2	92	23
5600****	53.7	1.53	2.8	5.12	9.4	5.97	11.5	88	22
	350	5.01	1.4	18.7	5.3	22.3	6.6	88	22
	1634	16.7	1.0	59.6	3.6	73.9	4.7	88	22

* Within-run (repeatability). Between Duplicate precision averaged over all runs

** Within-calibration. Total precision with weighted components of within-run, between–run and between-day variation

*** Within-lab. A measure of the effect of recalibration on total precision, calculated within reagent lot, using data from at least 4 calibrations

**** Performance characteristics for the VITROS 5600 System are applicable to the VITROS XT 7600 System.

Specificity

Substances that do not Interfere

The VITROS Estradiol test was evaluated for interference consistent with CLSI document EP7. [12] Of the compounds tested, none was found to cause a bias of >10% with the test at the concentrations indicated at estradiol concentrations of 1155–1262 pmol/L (315–344 pg/mL).

Compound	Concentration	
Biotin	20.5 nmol/L	0.5 µg/dL
Triolein	36.1 mmol/L	3200 mg/dL

Cross-Reactivity

The cross-reactivity of the VITROS Estradiol test was evaluated by adding the following substances to control samples containing no estradiol.

Cross-Reactant Tested	Concentration		Mean Value of Cross-reactant Pool		% Cross-reactivity
d-Equilenin	1.0 µmol/L	26.7 µg/dL	4697 pmol/L	1279 pg/mL	0.469
β-Estradiol-17-Valerate	2.8 µmol/L	99.8 µg/dL	9582 pmol/L	2610 pg/mL	0.342
Equilin	3.7 µmol/L	99.3 µg/dL	5761 pmol/L	1569 pg/mL	0.156
Estradiol-3-sulfate	750 nmol/L	28.1 µg/dL	833 pmol/L	227 pg/mL	0.111
17α-Ethynyl Estradiol	3.4 µmol/L	101.0 µg/dL	5292 pmol/L	1441pg/mL	0.156
Estrone-3-sulfate	1.9 µmol/L	70.8 µg/dL	399 pmol/L	109 pg/mL	0.021
17-αEstradiol	367 nmol/L	10.0 µg/dL	69.9 pmol/L	19.0 pg/mL	0.019
Estriol-3-sulfate	2.6 µmol/L	102.0 µg/dL	113 pmol/L	30.7 pg/mL	0.004
5α-Dihydro-testosterone	3.4 µmol/L	98.7 µg/dL	16.8 pmol/L	4.58 pg/mL	0.0005
Androstenedione	3.5 µmol/L	100.0 µg/dL	<10 pmol/L	<2.72 pg/mL	*
βEstradiol-3-sulfate-17β-Glucuronide	137 nmol/L	8.3 µg/dL	<10 pmol/L	<2.72 pg/mL	*
βEstradiol-17β-Glucuronide	201 nmol/L	9.5 µg/dL	<10 pmol/L	<2.72 pg/mL	*
Clomiphene Citrate	1.7 µmol/L	102.0 µg/dL	<10 pmol/L	<2.72 pg/mL	*
Cortisone	2.8 µmol/L	101.0 µg/dL	<10 pmol/L	<2.72 pg/mL	*
Danazol	740 nmol/L	25.0 µg/dL	<10 pmol/L	<2.72 pg/mL	*
DHEA-sulfate	2.3 µmol/L	89.8 µg/dL	<10 pmol/L	<2.72 pg/mL	*
Estriol-16α-(βD-Glucuronide)	1.9 µmol/L	92.4 µg/dL	<10 pmol/L	<2.72 pg/mL	*
Hydrocortisone	2.8 µmol/L	101.0 µg/dL	<10 pmol/L	<2.72 pg/mL	*
Mesterolone	821 nmol/L	25.0 µg/dL	<10 pmol/L	<2.72 pg/mL	*
Progesterone	3.2 µmol/L	100.6 µg/dL	<10 pmol/L	<2.72 pg/mL	*
Testosterone	347 nmol/L	10.0 µg/dL	<10 pmol/L	<2.72 pg/mL	*

* Concentration was below 10.0 pmol/L (2.72 pg/mL).

Cross-reactivity was expressed as the mean result obtained for the cross-reactant pool divided by the cross-reactant concentration in percentage term.

$$\% \text{ Cross-reactivity} = \frac{\text{Mean Result for the Cross-reactant Pool}}{\text{Concentration of Cross-reactant}} \times 100$$

Cross-Reactivity at 50% Displacement

Cross-reactivity at 50% displacement was calculated from the dose-response curves obtained for the cross-reactants and from the calibration curve for the VITROS Estradiol test. The concentrations at 50% displacement of the zero calibrator for the cross-reactant and for the VITROS Estradiol test were obtained from these curves.

Compound	% Cross-reactivity
Estrone	2.95
Estriol	0.52

$$\% \text{ Cross-reactivity at 50\% displacement} = \frac{\text{Concentration at 50\% displacement for Estradiol}}{\text{Concentration at 50\% displacement for Cross-reactant}} \times 100$$

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Glossary of Symbols

The following symbols may have been used in the labeling of this product.

Do Not Reuse	Upper Limit of Temperature	Range
Use by or Expiration Date (Year-Month-Day)	Lower Limit of Temperature	Range of Means
LOT Batch Code or Lot Number	Temperature Limitation	Midpoint
SN Serial Number	Consult Instructions for Use	Revised
REF Catalog Number or Product Code	Attention: The Instructions for Use (IFU) has been updated	Supersedes
Caution	S1 For use in Slide Supply 1	Contains Sufficient for "n" Tests
Keep Dry (Protect from Moisture/Humidity)	S2 For use in Slide Supply 2	IVD *in vitro* Diagnostic Medical Device
Manufacturer	SI SI Units	Der Grüne Punkt (the Green Dot). Manufacturer follows certain packaging material waste disposal management regulations
Date of Manufacture	CONV Conventional Units	Estimated within-lab SD
EC REP Authorized Representative in the European Community	Value	
Corrosive	Flammable	Serious Health Hazards
Health Hazards	Acute Toxicity	Environmental or Aquatic Toxicity

Revision History

Date of Revision	Version	Description of Technical Changes*
2020-04-10	9.0	• Warnings and Precautions: updated Hazard and Precaution Statements to align with the new Safety Data Sheets

* The change bars indicate the position of a technical amendment to the text with respect to the previous version of the document.

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Signature

Obsolete Date

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