VITROS® Immunodiagnostic Products

INSTRUCTIONS FOR USE CA125

VITROS Immunodiagnostic Products CA 125 II™ Reagent Pack	REF	680 0038
VITROS Immunodiagnostic Products CA 125 II™ Calibrators	REF	680 0034

Intended Use

For *in vitro* diagnostic use only.

VITROS Immunodiagnostic Products CA 125 II Reagent Pack

For the quantitative measurement of OC 125 defined antigen in human serum and plasma (EDTA or heparin) using the VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems.

VITROS Immunodiagnostic Products CA 125 II 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 OC 125 defined antigen in human serum and plasma (EDTA or heparin).

Summary and Explanation of the Test

CA 125 test concentrations are defined by using the OC 125 monoclonal antibody which was produced using lymphocytes from a mouse immunized with OVCA 433, a cell line derived from a papillary serous cystadenocarcinoma of the ovary.[1] The VITROS CA 125 II test is a second generation test for the detection of OC 125 defined antigen on a high molecular weight glycoprotein in serum. The test utilizes M11 monoclonal antibody, as the capture antibody that binds molecules containing OC 125 defined antigen.[2] These defined antigens are quantified using OC 125 antibody as conjugate. The OC 125 defined antigen, isolated from either cell culture or serum, are found on a heterogeneous, high molecular weight (200 to 1 000 kilodalton) glycoprotein. The antigen is proteinaceous in nature, but has non-determinant associated carbohydrate moieties.[3]

OC 125 defined antigen can be found in a high percentage of non-mucinous epithelial ovarian tumors[4] and is found in the serum of women bearing such tumors.[5-6] CA 125 test values are elevated in most patients with active epithelial ovarian cancer, including those with stage I disease. In addition, CA 125 test values are elevated in 1-2% of healthy individuals and may be elevated in diseases other than ovarian carcinoma, including both benign and malignant disorders. CA 125 test concentrations greater than or equal to 35 U/mL may be found in patients with non-malignant conditions, such as pericarditis, cirrhosis, severe hepatic necrosis, endometriosis (Stages II–IV), first trimester pregnancy, and ovarian cysts or in patients with non-ovarian malignancies, such as uterine carcinoma, hepatoma, pancreatic adenocarcinoma, and lung cancer.[5-10]

In women with primary epithelial ovarian carcinoma who have undergone first-line therapy and are candidates for diagnostic second-look procedures, a CA 125 test concentration greater than or equal to 35 U/mL has been found to be indicative of the presence of residual tumor.[11-13] Assuming the physician cannot identify alternative causes for an elevated CA 125 test concentration, a CA 125 test concentration determined to be greater than or equal to 35 U/mL provides substantial evidence that residual tumor is present. A CA 125 test concentration below 35 U/mL does not indicate the absence of residual ovarian cancer because patients with histopathologic evidence of ovarian carcinoma may have CA 125 test concentrations within the range of healthy individuals.[5,14-17] Clinical decisions should not be based on a VITROS CA 125 II test concentrations below 35 U/mL.

Principles of the Procedure

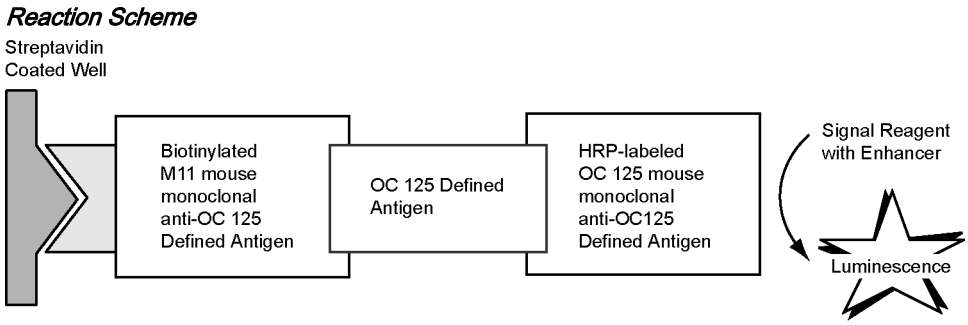
An immunometric immunoassay technique is used, which involves the simultaneous reaction of OC 125 defined antigen present in the sample with a biotinylated antibody (M11 mouse monoclonal anti-OC 125 defined antigen) and a horseradish peroxidase (HRP)-labeled antibody conjugate (OC 125 mouse monoclonal anti-OC 125 defined antigen). 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.[18] 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 OC 125 defined antigen present.

Test Type	System *	Incubation Time	Time to first result	Test Temperature	Reaction Sample Volume
Immunometric immunoassay	ECi/ECiQ, 3600, 5600, XT 7600	29 minutes	37 minutes	37 °C	25 µL

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

Reaction Scheme



Warnings and Precautions

WARNING: Potentially Infectious Material

Use caution when handling material of human origin. Consider all samples potentially infectious. No test method can offer complete assurance that hepatitis B virus, hepatitis C virus (HCV), human immunodeficiency virus (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). [19]

WARNING: Contains ProClin 300 (CAS 55965-84-9) [20]

The VITROS CA 125 II Reagent Pack contains 1% ProClin 300. H317: May cause an allergic skin reaction. P280: Wear protective gloves/protective clothing/eye protection/face protection. P302 + P352: IF ON SKIN: Wash with plenty of soap and water. P333 + P313: If skin irritation or rash occurs: Get medical advice/attention. P363: Wash contaminated clothing 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 ≥3 ng biotin/well)
- 9.4 mL conjugate reagent (HRP-mouse monoclonal anti-OC 125 defined antigen, binds ≥607 U OC 125 defined antigen/mL) in buffer with bovine serum albumin, bovine gamma globulin and antimicrobial agent
- 9.4 mL biotinylated antibody reagent (biotin-mouse monoclonal anti-OC 125 defined antigen, binds ≥607 U OC 125 defined antigen/mL) in buffer with bovine serum albumin, bovine gamma globulin 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 onto the system.
- Handle the reagent pack with care. Avoid the following:
  - allowing condensation to form on the pack
  - causing reagents to foam
  - agitation of the pack

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 CA 125 II 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 CA 125 II Calibrators 1, 2, and 3 (OC 125 defined antigen in buffer with bovine serum albumin and antimicrobial agent, 1.75 mL); nominal values 24.0; 130 and 875 U OC 125 defined antigen/mL
- Lot calibration card
- Protocol card
- 24 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 CA 125 II Calibrators are supplied ready for use.
- The VITROS CA 125 II 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 CA 125 II test uses 25 µL of calibrator for each determination. The VITROS CA 125 II 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.

Special Precautions

IMPORTANT:	Certain collection devices have been reported to affect other analytes and tests.[21] 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.[22-23]
- Thoroughly mix samples by inversion and bring to 15–30 °C (59–86 °F) before use.
- The VITROS CA 125 II 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.
- 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 7 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 CA 125 II Reagent Pack
- VITROS Immunodiagnostic Products CA 125 II Calibrators

Materials Required but Not Provided

- VITROS Immunodiagnostic Products Signal Reagent
- VITROS Immunodiagnostic Products Universal Wash Reagent
- VITROS Immunodiagnostic Products High Sample Diluent B Reagent Pack
- Quality control materials
- 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 or plasma (EDTA or heparin) samples with concentrations greater than the measuring range may be automatically diluted on the system up to 20-fold (1 part sample with 19 parts diluent) by the VITROS Immunodiagnostic and VITROS Integrated Systems with the VITROS High Sample Diluent B Reagent Pack prior to test. Refer to the VITROS High Sample Diluent B Reagent Pack instructions for use.

Default Test Name

The default test name which will appear on patient reports is CA 125 II. The default short name that will appear on the test selection menus and laboratory reports is CA125. 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 CA 125 II test is traceable to in-house reference calibrators which have been value assigned to correlate to another commercially available test.

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	5.5*–1000 U/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

Controls containing suitable levels of OC 125 are recommended for use with the VITROS Immunodiagnostic and VITROS Integrated Systems. The performance of 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 OC 125 defined antigen 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 CA 125 II 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. [24]

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 U/mL.

Limitations of the Procedure

Known Interfering Substances

The VITROS CA 125 II test was evaluated for interference consistent with CLSI document EP7. [25] Commonly encountered substances were tested on 2 lots of reagents. Of the compounds tested, none was found to cause a bias of >10%. Refer to "Specificity" for a list of compounds tested that did not show interference.

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. [26] 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.
- Individuals receiving mouse immunoglobulin by parenteral routes may produce anti-mouse antibodies. Serum from such individuals may produce erroneous results. [27- 28]
- The VITROS CA 125 II has no high dose hook effect up to 340,000 U/mL.
- Different test methods cannot be used interchangeably. OC 125 defined antigen in a given patient sample determined with different tests and from different manufacturers can vary due to differences in test methods and reagent specificity. A change to the test used during serial monitoring of a patient should be accompanied by additional sequential testing to confirm baseline values. The results reported by the laboratory to the physician must include the identity of the CA 125 II test used.
- CA 125 test concentrations are elevated in 1–2% of healthy individuals and may be elevated in diseases other than ovarian carcinoma, including both benign and malignant disorders. CA 125 test concentrations greater than or equal to 35 U/mL may be found in patients with non-malignant conditions, such as pericarditis, cirrhosis, severe hepatic necrosis, endometriosis (Stages II-IV), first trimester pregnancy, and ovarian cysts or in patients with non-ovarian malignancies, such as uterine carcinoma, hepatoma, pancreatic adenocarcinoma, and lung cancer. [5- 10]
- A CA 125 test concentration below 35 U/mL does not indicate the absence of residual ovarian cancer because patients with histopathologic evidence of ovarian carcinoma may have CA 125 test concentrations within the range of healthy individuals. [5, 14- 17] Clinical decisions should not be based on a VITROS CA 125 II test concentrations below 35 U/mL.
- The test should not be performed until at least three weeks after the completion of primary chemotherapy and at least two months after abdominal surgery. This is recommended because it is not clear what effect, if any, these procedures may have on the CA 125 test concentration.
- Biotin levels in serum remain elevated for up to 24 hours after oral or intravenous biotin administration. [29]

- Certain drugs are known to alter CA 125 concentrations *in vivo*. Please consult one of the published summaries for details. [30- 32]

Expected Values and Interpretation of Results

It is recommended that each laboratory establish its own expected values for the population it serves. As a guide, 98.5% of the VITROS CA 125 II test concentrations in a study of 200 samples from normal females were found to be 35 U/mL or less. Of 75 samples from patients with ovarian carcinoma, 54 samples had VITROS CA 125 II test concentrations above 35 U/mL.

Distribution of VITROS CA 125 II test concentrations

	N	≤35	35.1–65	65.1–100	>100
Healthy Subjects					
Normal Females	200	197	3	0	0
Normal Males	50	50	0	0	0
Non-Malignant Conditions					
Gynecological	50	48	1	1	0
Pregnancy	30	25	1	2	2
Gastrointestinal	30	28	1	0	1
Malignant Disease					
Ovarian	75	21	7	7	40
Gastrointestinal	30	21	2	1	6
Other*	40	32	2	0	6

* Bladder, Kidney, Breast, Pancreas and Colon

Units = U/mL

Interpretation of Results

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

Performance Characteristics

Limit of Detection

The limit of detection (LoD) for VITROS CA 125 II is 5.5 U/mL, determined consistent with NCCLS document EP17 [33] and with proportions of false positives (α) less than 5% and false negatives (β) less than 1%; based on 601 determinations, with 1 blank and 5 low-level samples. The Limit of Blank (LoB) is 2.9 U/mL. The data presented are a representation of the product performance.

Limit of Blank and Limit of Detection

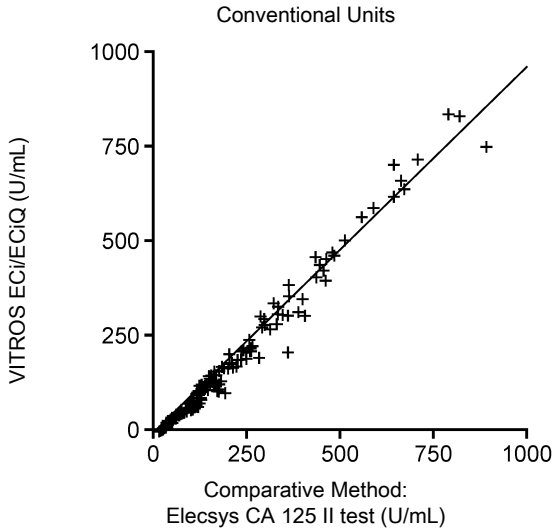
LoB	LoD*
U/mL	U/mL
2.9	5.5

* Proportions of false positives (α) and false negatives (ß) less than 5% and 1% respectively; based on 601 determinations, with 1 blank and 5 low-level samples.

Accuracy (Method Comparison)

Accuracy was evaluated consistent with NCCLS document EP9. [34] The plot 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 Elecsys CA 125 II test. The relationship between the 2 methods was determined by Passing and Bablok regression. [35]

The table also shows the results of method comparison studies [36] 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 Passing and Bablok regression. [35]



System	n	Slope	Correlation Coefficient	Conventional Units (U/mL) Range of Samples	Intercept
ECi/ECiQ vs. Comparative Method	250	0.963	0.946	8.53–998	0.654
3600 vs. ECi/ECiQ	102	0.950	0.999	7.21–960	-0.238
5600* vs. ECi/ECiQ	102	0.978	0.999	7.21–960	-0.434

* 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.[37] Two replicates each of 3 pools of patient serum 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.[38] Two replicates 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 = U/mL							No. Observ.	No. Days
	Mean CA 125 II Conc.	Within-run*		Within-calibration**		Within-lab***			
		SD	CV (%)	SD	CV (%)	SD	CV (%)		
ECi/ECiQ system 1	29.2	0.545	1.9	1.52	5.2	1.68	5.8	80	20
	94.0	1.58	1.7	4.20	4.5	5.01	5.3	80	20
	417	10.0	2.4	22.2	5.3	22.8	5.5	80	20
ECi/ECiQ system 2	28.1	0.451	1.6	1.20	4.3	1.12	4.0	80	20
	91.0	1.58	1.7	3.81	4.2	3.63	4.0	80	20
	414	4.52	1.1	18.2	4.4	17.9	4.3	80	20
3600	31.3	0.523	1.7	0.838	2.7	1.06	3.2	84	21
	99.5	1.29	1.3	2.21	2.2	2.77	2.7	84	21
	262	3.31	1.3	5.77	2.2	7.59	2.8	84	21
5600****	31.1	0.295	0.9	0.725	2.3	0.994	3.0	84	21
	97.4	1.01	1.0	2.46	2.5	2.82	2.7	84	21
	260	2.78	1.1	6.47	2.5	5.86	2.1	84	21

* 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 CA 125 II test was evaluated for interference consistent with CLSI document EP7.[25] Of the compounds tested, none was found to cause a bias of >10% with the test at the concentrations indicated at CA 125 II concentrations of 27.3–38.2 U/mL.

Compound	Concentration	
Acetaminophen	1323 µmol/L	200 µg/mL
Acetylsalicylic Acid	2.78 mmol/L	50 mg/dL
Ascorbic Acid	0.341 mmol/L	6 mg/dL
Bilirubin	0.342 mmol/L	20 mg/dL
Biotin	40.9 nmol/L	1 µg/dL
Chlorpromazine	28.1 µmol/L	1 mg/dL
Cisplatin	3.33 mmol/L	100 mg/dL
Cytoxan	0.896 mmol/L	25 mg/dL
Dexamethasone	3.44 µmol/L	135 µg/dL
Dimenhydrinate	21.3 µmol/L	1 mg/dL
Diphenhydramine	34.3 µmol/L	1 mg/dL
Doxorubicin	1.30 µmol/L	75 µg/dL
5-Fluorouracil	0.75 mmol/L	9.76 mg/dL
Hemoglobin	0.62 mmol/L	1000 mg/dL
Ibuprofen	3.39 mmol/L	70 mg/dL
Methotrexate	9.99 mmol/L	454 mg/dL
Metoclopramide	29.7 µmol/L	1 mg/dL
Taxol	0.88 µmol/L	75 µg/dL
Triolein	22.6 mmol/L	2000 mg/dL

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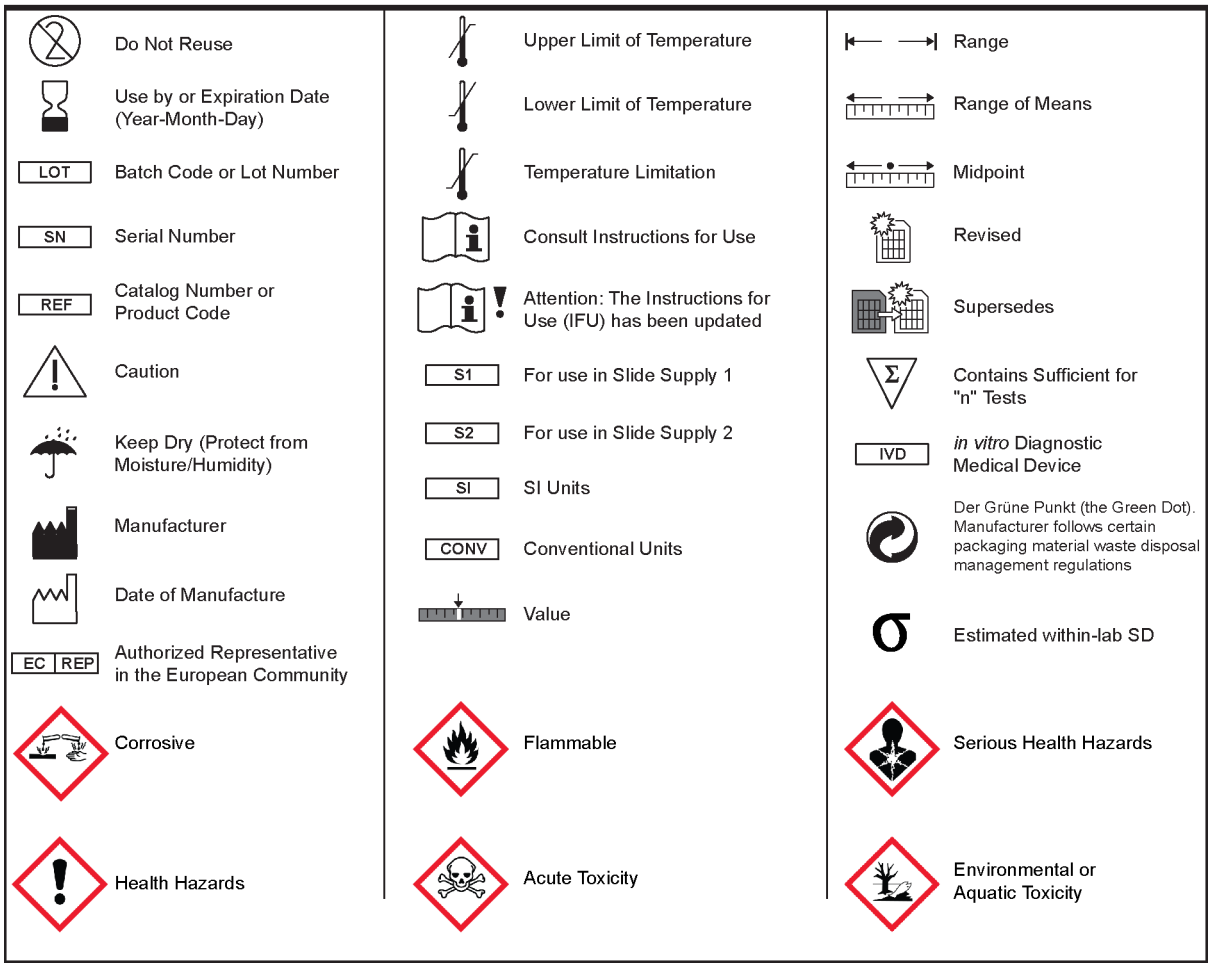
Glossary of Symbols

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



Revision History

Date of Revision	Version	Description of Technical Changes*
2019-09-06	9.1	• Glossary of Symbols: updated • Added EC Representative address
2017-09-27	9.0	• Added information for the VITROS XT 7600 Integrated System • Minor formatting and wording updates • References: updated • Glossary of Symbols: updated

* 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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