VIDAS® Progesterone (PRG)

IVD

The VIDAS® Progesterone (PRG) assay is intended for use on the instruments of the VIDAS family (VITEK® ImmunoDiagnostic Assay System) as an automated quantitative enzyme-linked fluorescent immunoassay (ELFA) for the determination of progesterone concentration in human serum or plasma (EDTA and lithium heparin). The VIDAS Progesterone (PRG) assay is intended for use as an aid in the diagnosis and treatment of disorders of the ovaries and placenta.

SUMMARY AND EXPLANATION OF THE TEST

Progesterone is one of the main steroid hormones secreted by the ovaries. Its level increases at the time of ovulation to reach its peak during the luteal phase; the uterus is then prepared for the implantation of a fertilized ovum (1) .

For patients at risk for abortion during the early weeks of pregnancy or in cases of suspected infertility, evaluating the progesterone level, and the levels of estradiol, LH and FSH enable ovulation and the luteal phase to be determined (2,3,4,5). In fact, abnormally low levels of progesterone may be found in cases of corpus luteum dysfunction, anovulation and short menstrual cycles (6,7).

PRINCIPLE OF THE PROCEDURE

The VIDAS Progesterone (PRG) assay is an enzyme-linked fluorescent immunoassay (ELFA) performed on an automated instrument. All assay steps and assay temperature are controlled by the instrument. A pipette tip-like disposable device, the Solid Phase Receptacle (SPR®), serves as a solid phase for the assay as well as a pipetting device.

At the time of manufacture, the SPR is coated with mouse monoclonal anti-progesterone antibodies. The VIDAS Progesterone (PRG) assay configuration prevents nonspecific reactions with the SPR. Reagents for the assay are located in the sealed Reagent Strips.

The sample is transferred into the well containing the progesterone derivative conjugated with alkaline phosphatase. The sample/conjugate mixture is cycled in and out of the SPR and the progesterone present in the sample competes with the progesterone-alkaline phosphatase conjugate for binding with the mouse anti-progesterone antibodies coated on the SPR. Wash steps remove unbound conjugate.

A fluorescent substrate, 4-methylumbelliferyl phosphate, is cycled through the SPR. Enzyme remaining on the SPR wall will catalyze the conversion of the substrate to the fluorescent product 4-methylumbelliferone (450 nm). The intensity of fluorescence is measured by the optical scanner in the instrument; it is inversely proportional to the progesterone concentration present in the sample.

When the VIDAS Progesterone (PRG) assay is completed, the results are analyzed automatically by the instrument, and a report is printed for each sample.

KIT COMPOSITION (60 tests) :

60 PRG Reagent Strips	STR	Ready to use.
60 PRG SPRs (2 x 30)	SPR	Ready to use, SPRs are coated with anti-progesterone monoclonal immunoglobulins (mouse).
PRG Control 1 x 3 ml (lyophilized)	C1	Reconstitute with 3 mL of distilled water. Wait for 5 to 10 minutes, then mix. After reconstitution, the control is stable for 2 weeks at 2-8°C or up to the expiration date given on the kit at -25 ± 6°C. 5 freezing/thawing cycles possible. Human serum* + progesterone + preservative. MLE data indicate the confidence interval in ng/mL ("Control C1 (+) Dose Value Range").
PRG Calibrator 2 x 4 ml (lyophilized)	S1	Reconstitute with 4 mL of distilled water. Wait for 5 to 10 minutes, then mix. After reconstitution, the calibrator is stable for 2 weeks at 2-8°C or up to the expiration date given on the kit at -25 ± 6°C. 5 freezing/thawing cycles possible. Human serum* + progesterone + preservative. MLE data indicate the concentration in ng/mL ("Calibrator (S1) Dose Value") and the confidence interval in "Relative Fluorescence Value ("Calibrator (S1) RFV Range).
Specifications for the factory master data required to calibrate the test: • MLE data (Master Lot Entry) provided in the kit, or • MLE bar code printed on the box label.		
1 Package Insert provided in the kit or downloadable from www.biomerieux.com/techlib.		

* This product has been tested and shown to be negative for HBs antigen, antibodies to HIV1, HIV2 and HCV. However, since no existing test method can totally guarantee their absence, this product must be treated as potentially infectious. Therefore, usual safety procedures should be observed when handling.

The SPR®

The interior of the SPR® is coated during production with anti-human µ chain antibodies (goat). Each SPR is identified by the "PRG" code. Only remove the required number of SPRs from the pouch and carefully reseal the pouch after opening.

The strip

The strip consists of 10 wells covered with a labeled, foil seal. The label comprises a bar code which mainly indicates the assay code, kit lot number and expiration date. The foil of the first well is perforated to facilitate the introduction of the sample. The last well of each strip is a cuvette in which the fluorometric reading is performed. The wells in the center section of the strip contain the various reagents required for the assay.

Description of the PRG Reagent Strip :

Wells	Reagents
1	Sample.
2-3-4	Empty wells.
5	Conjugate: alkaline phosphatase labeled progesterone derivative + 1g/l sodium azide (600 µl).
6	Wash buffer: TRIS-NaCl (0.05 mol/l) pH 7.4 + 1g/l sodium azide (600 µl).
7	Wash buffer: Sodium phosphate (0.1 mol/l) + NaCl (0.3 mol/l) pH 7.5 + 1g/l sodium azide (600 µl).
8	Diluent: Sodium phosphate (0.1 mol/l) pH 7.5 + protein stabilizer + 1g/l sodium azide (600µl).
9	Wash buffer: diethanolamine DEA* (1.1 mol/l, or 11.5 %) pH 9.8 + 1 g/l sodium azide (600 µl).
10	Reading cuvette with substrate : 4-Methyl-umbelliferyl-phosphate (0.6 mmol/L) + diethanolamine (DEA**) (0.62 mol/L or 6.6%, pH 9.2) + 1 g/l sodium azide (300 µl).

* Signal Word: **DANGER**

Hazard statement

H318 : Causes serious eye damage.
H373 : May cause damage to organs through prolonged or repeated exposure.
H315 : Causes skin irritation.
H302 : Harmful if swallowed.

Precautionary statement

P280 :Wear protective gloves/protective clothing/eye protection/face protection.
P305 + P351 + P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P309 + P311 : IF exposed or if you feel unwell: Call a POISON CENTER or doctor/physician.

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For further information, consult the Safety Data Sheet.

MATERIALS REQUIRED BUT NOT PROVIDED

- Pipettor with disposable tips that will dispense 4 ml, 3 ml and 200 µl.
- Powderless disposable gloves.
- For other specific materials, please refer to the Instrument Operator's Manual.
- Instrument of the VIDAS family.

WARNINGS AND PRECAUTIONS

For *In Vitro* Diagnostic Use.
For professional use only.

- This kit contains products of human origin. No known analysis method can totally guarantee the absence of transmissible pathogenic agents. It is therefore recommended that these products be treated as potentially infectious and handled observing the usual safety precautions (see Laboratory biosafety manual - WHO - Geneva - latest edition).
- Consider all patient specimens potentially infectious and observe routine biosafety precautions. Dispose of all used components and other contaminated materials by acceptable procedures for potentially biohazardous human blood products.
- This kit contains products of animal origin. Certified knowledge of the origin and/or sanitary state of the animals does not totally guarantee the absence of transmissible pathogenic agents. It is therefore recommended that these products be treated as potentially infectious and handled observing the usual safety precautions (do not ingest or inhale).
- Do not mix reagents or disposables from different lots.
- Powderless gloves are recommended as powder has been reported as a cause of false results in some enzyme immunoassays.
- Kit reagents contain 1g/L sodium azide which could react with lead or copper plumbing to form explosive metal azides. If any liquid containing sodium azide is disposed of in the plumbing system, drains should be flushed with water to avoid build-up.
- The wash buffer (well 9) contains a harmful agent (11.5% diethanolamine). Refer to the hazard statements "H" and the precautionary statements "P" above.
- The substrate (well 10) contains an irritant agent (6.6% diethanolamine). Refer to the hazard statements "H" and the precautionary statements "P" above.
- Spills should be wiped thoroughly after treatment with liquid detergent and a solution of household bleach containing at least 0.5 % sodium hypochlorite to inactivate infectious agents. See the Operator's Manual for cleaning spills on or in the instrument. Do not place solutions containing bleach in the autoclave.
- The instrument should be routinely cleaned and decontaminated. See the Operator's Manual for the appropriate procedures.

STORAGE AND HANDLING

- Store the VIDAS® Progesterone (PRG) kit at 2-8°C. **Do not freeze the SPR®s or the reagent strips.** Return unused components to 2-8°C.
- After opening the kit, check that the SPR pouch is correctly sealed and undamaged. If not, do not use the SPRs.
- Carefully reseal the pouch with the desiccant inside after use to maintain stability of the SPRs and return the complete kit to 2-8°C.
- All components are stable, when stored appropriately, until the expiration date printed on the label. Do not use components beyond the expiration date.

SPECIMEN COLLECTION AND PREPARATION

Acceptable specimens include serum or plasma (EDTA or lithium heparin). The use of heat-inactivated sera has not been established for this test, do not heat sera. Samples can be stored at 2-8°C in stoppered tubes for up to 48 hours. If storage for longer than this is required, freeze samples at - 25 ± 6°C for up to two months. Do not repeatedly freeze and thaw samples.

INSTRUCTIONS FOR USE

For complete instructions, see the User's Manual.

Reading Master lot data

Before each new lot of reagents is used, enter the specifications (or factory master data) into the instrument using the master lot entry (MLE) data.
If this operation is not performed **before initiating the tests**, the instrument will not be able to print results.

Note: the master lot data need only be entered once for each lot.
It is possible to enter MLE data **manually or automatically** depending on the instrument (refer to the User's Manual).

Calibration

Calibration, using the calibrator provided in the kit, must be performed each time a new lot of reagents is opened, after the master lot data have been entered. Calibration should then be performed every 14 days. This operation provides instrument-specific calibration curves and compensates for possible minor variations in assay signal throughout the shelf-life of the kit.
The calibrator, identified by "S1", must be tested **in triplicate** (see Operator's Manual). The calibrator value must be within the set RFV "Relative Fluorescence Value" range. If this is not the case, recalibrate.

Assay procedure

1. Remove necessary components from the kit and return all unused components to storage at 2 - 8°C.
2. Allow components to reach room temperature (approximately 30 minutes).
3. Use one "PRG" strip and one "PRG" SPR for each sample, control or calibrator to be tested. **Make sure the storage pouch has been carefully resealed after the required SPRs have been removed.**
4. The test is identified by the "PRG" code on the instrument. The calibrator must be identified by "S1", and tested **in triplicate**. If the control is to be tested, it should be identified by "C1".
5. If needed, label "PRG" Reagent Strips with the appropriate sample identification numbers.
6. Mix the calibrator, control, and samples using a Vortex-type mixer (for serum or plasma separated from the pellet) .
7. **For this test, the calibrator, control, and sample test portion is 200 µl.**
8. Insert the "PRG" Reagent Strips and SPRs into the appropriate position on the instrument. Check to make sure the color labels with the assay code on the SPRs and the Reagent Strips match.

9. Initiate the assay processing as directed in the Operator's Manual. All steps will be executed automatically by the instrument.
10. Reclose the vials and return them to the required temperature after pipetting.
11. The assay will be completed within approximately 45 minutes. After the assay is completed, remove the SPRs and strips from the instrument.
12. Dispose of the used SPRs and strips into an appropriate recipient.

RESULTS AND INTERPRETATION

Two instrument readings for fluorescence in the Reagent Strip's reading cuvette are taken for each specimen tested. The first reading is a background reading of the cuvette and substrate before the SPR is introduced into the substrate. The second reading is taken after the substrate has been exposed to the enzyme conjugate remaining on the interior of the SPR®. The background reading is subtracted from the final reading to give a Relative Fluorescence Value (RFV) for the test result.
Once the assay is completed, results are automatically calculated by the instrument using a calibration curve stored in memory, and then printed. PRG concentrations are expressed in ng/ml.

Samples with a PRG concentration greater than 80 ng/mL must be retested after a 1/2 dilution (1 volume of sample and 1 volume of Serum Free reagent ref.66 581).

A report is printed which records :
- the type of test performed,
- the sample identification,
- the date and time,
- the lot number and the expiration date of the reagent kit being used,
- each sample's RFV and progesterone concentration.

QUALITY CONTROL

A control is included in each VIDAS Progesterone (PRG) kit.
This control must be performed immediately after opening a new kit to ensure that reagent performance has not been altered. Each calibration must also be checked using this control.
The instrument will only be able to check the control value if it is identified by C1.
Results cannot be validated if the control value deviates from the expected values.

Note

It is the responsibility of the user to perform Quality Control in accordance with any local applicable regulations.

LIMITATION OF THE TEST

Samples collected from patients receiving mouse monoclonal antibodies, for diagnostic or therapeutic purposes, may contain human anti-mouse antibodies (HAMA). These samples may give falsely high or low results when tested with assay kits using mouse antibodies.
For diagnostic purposes, the VIDAS Progesterone (PRG) Assay results should be used in conjunction with other information gathered by the physician. e.g. symptoms, current drug therapy, clinical observations, other examinations, etc.
In cases of steroid therapy particularly micronized progesterone therapy, elevated progesterone results may be obtained.

PERFORMANCE DATA

Immunological Specificity

The cross-reactivity percentage is the ratio between the progesterone concentration and the compound concentration to be tested at 50% binding.

Tested components	Cross-reactivity percentage
Progesterone	100 %
20 α hydroxyprogesterone	0.03 %
6 β hydroxyprogesterone	0.29%
16 α hydroxyprogesterone	0.20 %
5 β dihydroxyprogesterone	17.39 %
5 α dihydroxyprogesterone	12.95 %
17 α hydroxyprogesterone	1.18 %
Deoxycorticosterone	1.15 %
Corticosterone	0.09 %
Testosterone	0.01 %
Estrone	0.01 %
Estradiol, Estriol	< 0.01 %

Detection limit

The detection limit (assay sensitivity) defined as the lowest concentration of progesterone that can be distinguished from zero concentration with a probability of 95% is 0.25 ng/ml.

Measurement range

The calibration range of the VIDAS® Progesterone (PRG) kit is 0.25 – 80 ng/ml.

PRECISION/REPRODUCIBILITY

Intra-assay precision

Five samples were tested for intra-assay precision. Thirty replicates of each sample were tested in the same run.

Sample	1	2	3	4	5
Mean concentration (ng/ml)	0.46	2.21	10.14	21.66	45.10
% CV	14.30	5.71	3.75	3.76	3.97

Inter-assay reproducibility on the same instrument

Five samples were tested in 29 runs on the same instrument over an 8-week period (recalibration was performed every 14 days as described in the Operator's Manual).

Sample	1	2	3	4	5
Mean concentration (ng/ml)	0.4	2.22	9.97	21.93	44.96
% CV	24.3	6.2	3.7	3.8	3.1

Inter-instrument inter-assay reproducibility

Five samples were tested singly in 8 runs on different instruments.

Sample	1	2	3	4	5
Mean concentration (ng/ml)	0.32	2.09	9.38	20.61	42.24
% CV	16.09	5.88	5.30	4.46	5.39

PARALLELISM (Dilution Tests)

Three samples were diluted in Serum Free human serum and tested singly in 3 runs. The mean concentration compared to the expected mean concentration is shown below.

Sample	Dilution factor	Expected values (ng/ml)	Measured values (ng/ml)	Recovery percentage
1	1/1	8.35	8.35	100.0%
	½	4.17	3.93	94.2
	¼	2.09	2.09	100.0
	1/8	1.04	1.05	101.0
	1/16	0.52	0.63	120.8
2	1/1	17.23	17.23	100.0
	½	8.62	8.80	102.1
	¼	4.31	4.17	96.9
	1/8	2.15	2.14	99.2
	1/16	1.08	1.07	99.7
3	1/1	38.84	38.84	100.0
	½	19.42	18.64	96.0
	¼	9.71	9.10	93.7
	1/8	4.86	4.55	93.7
	1/16	2.43	2.48	102.0

RECOVERY TESTS

Three samples were spiked with known quantities of progesterone (ng/ml) and tested singly in 3 runs. The measured mean concentration compared to the expected mean concentration is shown below.

Sample	Amount spiked (ng/ml)	Expected mean concentration (ng/ml)	Measured mean concentration (ng/ml)	Mean recovery percentage
1	0	0.4	0.4	100.0
	8.6	8.8	8.6	97.7
	13.0	13.2	13.1	98.9
	22.0	22.2	22.3	100.5
	28.8	29.0	28.1	97.0
	35.2	35.4	35.2	99.3
2	0	0.4	0.4	100.0
	8.7	8.9	9.8	110.3
	13.0	13.2	14.7	111.0
	22.0	22.2	25.3	114.1
	28.8	29.0	33.2	114.6
	35.2	35.5	40.8	115.1
3	0	3.4	3.4	100.0
	8.7	10.4	10.9	105.1
	13.0	14.7	15.0	101.8
	22.0	23.7	24.9	105.2
	28.8	30.5	32.8	107.4
	35.3	37.0	40.3	109.1

INTERFERENCE STUDIES

Method of Collection

Blood samples were collected from thirty patients. For each patient, 5 specimens were collected at the same time in a dry glass tube, in a tube with separating gel, in a dry silicone tube, in a lithium heparin tube, and in a tube with EDTA, respectively. Each sample collected was tested singly and sera from the same donor was tested in the same run. The dry glass tube was the reference to which the other methods were compared. The statistical ratio method that was used to evaluate the data showed that there was no significant difference with any of the specimen collection devices tested.

Lithium Heparin

Three pools of human sera were spiked with increasing quantities of lithium heparin.

		Amount of lithium heparin spiked (IU/ml)			
		0	0.5	5	50
Progesterone (ng/ml)	Pool 1	3.37	3.36	3.51	3.41
	Pool 2	7.54	7.93	7.89	7.79
	Pool 3	16.79	16.38	15.98	16.37

EDTA

Three pools of human sera were spiked with increasing quantities of EDTA.

		Amount of EDTA spiked (mg/ml)			
		0	1	5	10
Progesterone (ng/ml)	Pool 1	3.37	3.32	3.61	3.82
	Pool 2	7.54	7.95	8.44	8.39
	Pool 3	16.79	16.83	17.21	17.01

Hemoglobin

Three pools of human sera were spiked with increasing quantities of hemoglobin obtained from a lysate of human red blood cells.

		Amount of hemoglobin spiked (µmol/l)						
		0	15	30	60	150	186	300
Progesterone (ng/ml)	Pool 1	3.23	3.24	3.43	3.38	3.22	3.31	3.27
	Pool 2	7.53	7.80	7.98	7.78	7.61	7.43	7.59
	Pool 3	16.00	16.58	16.62	16.68	16.34	16.78	16.10

Lipids

Three pools of human sera were spiked with increasing quantities of a lipid solution.

		Amount of triglycerides spiked (g/l)				
		0.0	0.25	0.5	1.0	2.0
Progesterone (ng/ml)	Pool 1	3.23	3.10	3.34	3.48	3.23
	Pool 2	7.53	7.63	7.63	7.93	7.75
	Pool 3	16.00	16.33	15.89	16.38	16.02
Appearance		Clear	Opalescent		Turbid	

Bilirubin

Three pools of human sera were spiked with increasing quantities of bilirubin.

		Amount of bilirubin spiked (µmol/l)						
		8	31	58	120	287	362	591
Progesterone (ng/ml)	Pool 1	3.13	3.23	3.37	3.32	3.05	3.05	2.91
	Pool 2	7.3	7.49	8.14	7.64	7.14	7.24	6.74
	Pool 3	16.49	16.04	16.31	15.32	15.27	14.43	15.22

Although interference linked to the presence of hemoglobin, bilirubin or lipids has not been observed at the concentrations tested, using hemolyzed, icteric or lipemic samples is not recommended. If possible, collect a new specimen.

EXPECTED VALUES

A study was performed at bioMérieux (Marcy l'Etoile, France) using a population of healthy people. The following values were found (ranges mentioned below are the range within 95% confidence limits of results observed in this study, and are given as guidelines only):

	# of Samples	Normal Range
Men:	49	<0.25 - 0.56 ng/ml
Women:		
· Follicular phase	135	<0.25 - 0.54 ng/ml
· Luteal Phase	124	1.5 - 20.0 ng/ml
· Ovulation	53	<0.25 - 6.22 ng/ml
· Menopause	26	<0.41 ng/ml

It is advisable for each laboratory to establish its own reference values from a well-defined population.

CORRELATION

Two hundred thirty-one samples were tested in-house. Samples with progesterone concentrations ranging from <0.25ng/ml to 80 ng/ml were tested using the VIDAS® Progesterone (PRG) Assay and a commercially available radioimmunologic assay kit. The data shows that the VIDAS Progesterone (PRG) correlated well with the RIA assay, as indicated by a slope of 0.921 and a correlation coefficient of 0.984. The results of the correlation are shown below:

Number of Samples	Equation of the Line	Correlation coefficient
231	y = 0.9214x + -0.018	0.984

WASTE DISPOSAL

Dispose of used or unused reagents as well as any other contaminated disposable materials following procedures for infectious or potentially infectious products.
It is the responsibility of each laboratory to handle waste and effluents produced according to their nature and degree of hazardousness and to treat and dispose of them (or have them treated and disposed of) in accordance with any applicable regulations.

LITERATURE REFERENCES

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INDEX OF SYMBOLS

Symbol	Meaning
REF	Catalog number
IVD	*In Vitro* Diagnostic Medical Device
	Manufacturer
	Temperature limit
	Use by date
LOT	Batch code
	Consult Instructions for Use
	Contains sufficient for <n> tests
	Date of manufacture

WARRANTY

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REVISION HISTORY

Change type categories :

N/A	Not applicable (First publication)
Correction	Correction of documentation anomalies
Technical change	Addition, revision and/or removal of information related to the product
Administrative	Implementation of non-technical changes noticeable to the user
Note:	*Minor typographical, grammar, and formatting changes are not included in the revision history.*

Release date	Part Number	Change Type	Change Summary
2015/01	13685C	Administrative	INDEX OF SYMBOLS REVISION HISTORY
		Technical	KIT COMPOSITION (60 tests) WARNINGS AND PRECAUTIONS
2015/06	13685D	Technical	CONTENT OF THE KIT (60 TESTS) INSTRUCTIONS FOR USE

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