# Instructions for Use
# Progesterone (CLIA)

**[Product Name]**

Progesterone (CLIA)

**[Packing Size]**

24×1 Tests/Pkg (Calibrators included); 60×1 Tests/Pkg (Calibrators included); 60×1 Tests/Pkg

**[Intended Use]**

Progesterone assay is used to quantitatively measure progesterone concentration in human serum, plasma, and whole blood samples, and is mainly used for auxiliary diagnosis of threatened miscarriage in the clinics [1, 2].

Progesterone belongs to the family of steroid hormones. It has a molecular mass of 314.5 Da. Progesterone is mainly produced by the corpus luteum of the ovary and the placenta during pregnancy. After being released into the blood, it binds to albumin and sex hormone-binding protein, and circulates in the blood stream. Normal men and women produce low levels of progesterone during the follicular phase, and progesterone levels are associated with the development and atrophy of the corpus luteum. The main function of progesterone is to prepare the uterus for the implantation of a fertilized egg, and to maintain pregnancy. During the follicular phase of the menstrual cycle, progesterone levels are low. After ovulation, progesterone produced by the corpus luteum rises rapidly, and reaches a maximum concentration of 10~20 ng/mL in 5 to 7 days after ovulation, making the endometrium change from a hyperplasia state to a secretory state. In the last 4 days of the menstrual cycle, the corpus luteum shrinks and progesterone concentration decreases. If conception occurs, the corpus luteum does not atrophy and continues to secrete progesterone, keeping progesterone at levels equivalent to those of the mid-luteal phase until the sixth week of pregnancy. During pregnancy, the placenta gradually becomes the main source of progesterone, with concentration increasing from 10~50 ng/mL in the first 3 months of pregnancy to 50~280 ng/mL in the 7th to 9th months. Clinical studies have shown that progesterone plays a role in promoting ovulation and maintaining the normal function of the corpus luteum in non-pregnant women. If the corpus luteum produces insufficient progesterone, it may indicate insufficient corpus luteum function, which is associated with infertility and early miscarriage.

Elevated progesterone in blood can be seen in the following situations: (1) observe the time of ovulation and the production of progesterone in women: On days -1, 0, and +1 of ovulation, progesterone doubles, indicating ovulation. (2) During normal pregnancy, twin and multiple pregnancy, the amount of progesterone synthesis increases significantly, and the level of progesterone in blood is relatively elevated. (3) During pregnancy toxemia, preeclampsia, hydatidiform mole, and essential hypertension, the progesterone will also increase.

Reduced progesterone levels in blood are seen in the following situations: (1) threatened abortion, ectopic pregnancy, premature labor, amenorrhea, and infertility. (2) When luteal insufficiency and ovarian luteal hypoplasia occur, the progesterone decreases accordingly. (3) Serious imbalance of adrenal and thyroid functions may also affect ovarian function, cause ovulation disorders, and reduce progesterone generation accordingly.

**[Principle of the Assay]**

This immunoassay adopts a competition format. The test principle is as follows:

(1) Sample, reaction diluent and acridinium-labeled anti-PROG antibody are added to the reaction well. After mixing and incubation, PROG in the sample is bound by the acridinium-labeled anti-PROG antibody.

(2) Magnetic microparticle coated with PROG derivative is added to the reaction well, unreacted acridinium-labeled anti- PROG antibody will bind to the magnetic microparticle coated with the PROG derivative, while the PROG bound antibody in the sample can no longer bind to the magnetic microparticle coated with the PROG derivative, and is washed off after a magnet is used to capture the microparticle

(3) A photomultiplier tube is used to measure photons generated from the reaction. The count is inversely proportional to PROG concentration in the sample. The concentration of PROG is determined by an internal calibration curve.

**[Main Components]**

**Packing Size**

| Component \ Packing Size | | Fill Volume | | |
|---|---|---|---|---|
| | | 24×1 Tests/Pkg (Calibrators included) | 60×1 Tests/Pkg (Calibrators included) | 60×1 Tests/Pkg |
| PROG Reagent Cartridge | Microparticle (R1) | 24×50μL | 60×50μL | 60×50μL |
| | Conjugate (R2) | 24×100μL | 60×100μL | 60×100μL |
| | Reaction diluent (R3) | 24×100μL | 60×100μL | 60×100μL |
| PROG Calibrator | PROG Calibrator C1 | 1×1.0mL | 1×1.0mL | / |
| | PROG Calibrator C2 | 1×1.0mL | 1×1.0mL | / |
| Calibration Card | Calibration curve and calibrator information | 1 pcs | 1 pcs | / |

**Main Composition**

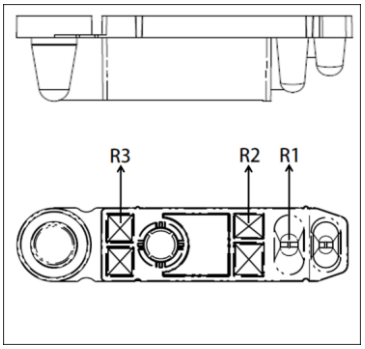
| Component | Main Composition | |
|---|---|---|
| PROG Reagent Cartridge | Microparticle (R1) | Magnetic microparticle coated with PROG derivative, ~0.15g/L; Tris buffer, 50 mmol/L; ProClin 300, 0.5g/L |
| | Conjugate (R2) | Acridinium labeled mouse anti- PROG antibody, ~200 μg/L; MES buffer, 50mmol/L; ProClin 300, 0.5g/L |
| | Reaction diluent (R3) | Tris buffer, 50mmol/L; ProClin 300, 0.5g/L |
| PROG Calibrator C1 | Progesterone; Tris buffer, 50mmol/L; ProClin 300, 0.5g/L | |
| PROG Calibrator C2 | Progesterone; Tris buffer, 50mmol/L; ProClin 300, 0.5g/L | |
| Calibration Card | Calibration curve and calibrator information | |

Note: (1) Components in different lots of reagent cannot be mixed or exchanged for use.

(2) Traceability: This quantification method can be traced back to WHO Reference material, Code: BCR-348R from NIBSC (National Institute for Biological Standard and control).

(3) Information about calibrators can be found in the instrument after scanning the Calibrator Card (such as lot number and concentration etc.)

The position of each component is shown in the front view (Upper) and vertical views (Down) of the reagent pack.



**Instruments and accessories needed but not supplied (available from Medcaptain)**

(1) Medcaptain Immu F6/F6S automatic chemiluminescent immunoassay analyzers;
(2) Pre-trigger solution;
(3) Trigger solution;
(4) Washing solution;
(5) 500μL pipette tips;
(6) Sexual Hormone Controls;
(7) Sample diluent.

**[Storage and Shelf-life]**

Storage: Store sealed reagent cartridges and calibrators at 2~8℃ in upright position, and avoid freezing.
Shelf Life: 14 months.
Stability of Calibrators: Sealed vial of calibrators can be kept at 2~8℃ in dark for 14 months. After calibrator C1 and C2 is uncapped, it can be stored for at 10~30℃ for 5 days, and at 2~8℃ for 60 days.
The dates of manufacturing and expiration can be found on the labels.

**[Matched Instruments]**

Medcaptain Immu F6/F6S automatic chemiluminescent immunoassay analyzers

**[Specimen Types]**

Serum, plasma sample and whole blood (collected with EDTA-$K_2$, EDTA-$K_3$, lithium heparin, and sodium heparin as the anti-coagulants) can be used in the testing.
Sample volume for each test: 30μL.
The collected sample should be tested as soon as possible.
Whole blood can be kept at 10~30℃ for 4 hours, and it is recommended to complete the sample testing within 4 hours after sample collection.
Serum and plasma can be kept at 10~30℃ for 12hours, at 2~8℃ for 5 days, and at -20℃ or below for 6 months. Frequent freeze-thaw cycles should be avoided, and only one freeze-thaw cycle is allowed. If the sample contains precipitate or frozen floccule, centrifugation is needed to clear the sample before testing.
Sample collection tubes from different manufacturers may lead to variation in testing results, due to the difference in tube material and additives in the tubes. Medcaptain has not evaluated all types of sample collection tubes from different manufacturers. Each laboratory should make its own judgment about the usability of sample collection tubes.

**[Test Procedure]**

**Reagent Preparation**

Reagent: PROG reagent cartridge (containing magnetic microparticle R1, acridinium labeled conjugate R2, and reaction diluent R3) is ready to use. It can be loaded directly into instrument after taken out of the package.
Calibrators: Calibrator C1 and C2 are ready for use. Each calibrator can be added to a sample cup, and then loaded to a sample rack. The sample rack can be pushed directly into the instrument for calibrator testing.

**Calibration**

Refer to the operation manual of each chemiluminescent immunoassay analyzer.
Calibration tests should be ordered before the first time use of PROG assay. Medcaptain provides PROG reagent pack and matched calibrators to calibrate the instrument.
Before calibration, scan the calibration card provided in the kit, the calibration curve and calibrator information are scanned into the system.
Before calibrator testing, take out reagent cartridges from the package, and load all of them into the instrument. The instrument scans two-dimensional barcode on the reagent pack automatically to obtain information of the reagent (reagent name, Lot No., and expiration date etc.);
Put calibrators on a sample rack, load the sample rack into the instrument.
On the screen interface of “Reagent > Request Calibration”, select test name and lot number to request a calibration.
Select the position of each calibrator on the sample rack, set the number of repeat tests, start calibration.
Automatic immunoassay analyzer makes use of calibration test data to validate the calibration curve, and adjust the calibration curve automatically.
Instrument calibration is effective for 60 days.
A new calibration is needed in the following situation:

(1) Change into a new lot of reagent;
(2) Control test results are out of the target range;
(3) The reagent lot has been used on the same instrument for more than 60 days.

Refer to the Chapter of “Calibration” in the instruction manual of Automatic Chemiluminescent Immunoassay Analyzer for detailed information about calibration.

**Control Testing**

Sexual hormone controls are matched with PROG reagent pack. There are two levels of controls: Low Control (L) and High Control (H).
These two-level controls should be tested in accordance with any local applicable regulations. Control testing is highly recommended every time the lot of reagent has been changed, the instrument has been re-calibrated, or after trouble shooting/ maintenance service.
Before the control testing, take out reagent cartridges from the package, and load all of them into the instrument. The instrument scans two-dimensional barcode on the reagent pack automatically to obtain information of the reagent (reagent name, Lot No., and expiration date etc.);
Put controls on a sample rack, and load the sample rack into the instrument;
Select “Control” on the interface of test menu, select test name and control lot;
Click on Start, and begin the testing. Check the results after control test is finished.
Control test results should fall into a specific range. If it is out of the target range, the user should check the system, such as expiration date of the controls, storage condition, instrument performance and status. After root cause analysis and correction, the user should test controls again. If the same problem exists, please contact customer service of Medcaptain.
Each laboratory should set up its own control range and frequency of control testing, based on its own practice.
Refer to the Chapter of “Control Testing” in the instruction manual of Automatic Chemiluminescent Immunoassay Analyzer for detailed information about control testing.

**Sample Testing**

Before sample testing, take out reagent cartridges from the package, and load all of them into the instrument. The instrument scans two-dimensional barcode on the reagent pack automatically to obtain information of the reagent (reagent name, Lot No., and expiration date etc.);
If a sample collection tube is directly loaded to the instrument for testing, the sample volume should be at least 1.0mL;
Uncap sample collection tubes, put samples on a sample rack, and push it into the instrument;
Select “Sample” on the interface of test menu, enter information of samples, select test name;
Click on Start, and begin the testing. Check the results after sample test is finished.
The reagent usage for each test is: R1 50 μL, R2 100 μL, and R3 50 μL. The instrument aspirates and mixes each component of the reagent cartridge, and incubate at 37℃. Time duration from sampling to result is about 19 min.
Refer to the Chapter of “Sample Testing” in the instruction manual of Automatic Chemiluminescent Immunoassay Analyzer for detailed information about sample testing.

**Result Calculation**

Based on the built-in calibration curve, the instrument automatically calculate the quantity of each sample，in a unit of ng/mL.

**[Reference Intervals]**

Samples for the study of reference interval were collected from 125 male and 141 postmenopausal healthy women in the age of 50~, 404 healthy pregnant women with age in 17~45, and 427 women with age in 17~45. None of them were using any hormonal contraception

For healthy women, the following reference intervals were obtained.

| Reference Individuals | Number | 5th percentile (ng/mL) | Median (ng/mL) | 95th percentile (ng/mL) |
|---|---|---|---|---|
| Healthy male | 125 | <0.10 | 0.12 | 0.23 |
| Healthy woman | | | | |
| Follicular phase | 125 | <0.10 | 0.20 | 0.9 |
| Ovulation | 167 | 0.10 | 0.51 | 12.12 |
| Luteal phase | 135 | 1.80 | 10.24 | 23.12 |
| Post-menopause | 141 | <0.10 | <0.10 | 0.12 |
| Healthy pregnant woman | | | | |
| Early pregnancy | 125 | 11.05 | 24.04 | 44.34 |
| Second trimester | 140 | 25.25 | 47.56 | 83.3 |
| Late pregnancy | 139 | 58.7 | 107.1 | 214.2 |

Due to the differences in geography, race, sex, and age of tested population, the reference interval may vary in different laboratories. It is highly recommended for each clinical lab to establish its own reference intervals.

**[Interpretation of Test Results]**

The test data is for clinical reference only. It cannot be used as the only confirmatory evidence nor to eliminate the possibility of diseases. Clinical diagnosis of patients should take clinical symptoms, body sign, disease history, other lab test results, and treatment response into comprehensive consideration.

The measurement range of this assay is: 0.1~50 ng/mL. If PROG concentration is lower than LoD, it will be reported as < 0.1 ng/mL; If PROG concentration is over the upper limit，it will be reported as > 50 ng/mL.

For a sample with PROG concentration of >50 ng/mL, sample diluent can be used to dilute the sample manually (a dilution factor of 1:10 is recommended). Test the diluted samples in duplicate if more accurate result is needed.

When the instrument shows a warning sign of “SMPL”, it means insufficient sample volume. Make sure enough sample volume is added for repeating the test. When the instrument shows a warning sign of “SMPJ”, it means the sample probe has been blocked. Clean sample clot in the probe before repeating the test.

Some results are tagged with signs. Refer to the Chapter of “Result Signs” in the instruction manual of Automatic Chemiluminescent Immunoassay Analyzer for detailed information about results tagged with signs.

**[Limitations of the Test Method]**

The test data is for clinical reference only. It cannot be used individually as the evidence to confirm or eliminate the possibility of diseases.

For endogenous interference substance with concentration less than the value shown in the table below, measurement error caused by the interference is within ±10%.

| Endogenous Interference Substance | Concentration of Interference Substance |
|---|---|
| Total Protein | ≤ 12 g/dL |
| Bilirubin | ≤ 75 mg/dL |
| Hemoglobin | ≤ 1000 mg/dL |
| Triglyceride | ≤ 500 mg/dL |

PROG samples around 20 ng/mL were tested when the potential cross-reactant at the following concentration, and the mean of the measurement results was within the mean (M) ± 2*standard deviation (SD) of the PROG sample with without cross-reactant.

| Cross reactant | Concentration | Cross reactant | Concentration |
|---|---|---|---|
| Corticosterone | 10 ng/mL | Aldosterone | 1000 ng/mL |
| 17α-Hydroxyprogesterone | 10 ng/mL | Danazol | 100000 ng/mL |
| 11-Deoxycorticosterone | 10 ng/mL | Clomiphene Citrate | 100 ng/mL |
| Pregnenolone | 16000 ng/mL | 11-Deoxycortisol | 6000 ng/mL |
| Cortisol | 20000 ng/mL | Phenylbutazone | 15000 ng/mL |
| 17β-Estradiol | 400 ng/mL | Testosterone | 2000 ng/mL |
| Estrone | 10 ng/mL | 6α-Methylprednisolone | 1000 ng/mL |
| Estriol | 400 ng/mL | / | / |

Heterophilic antibodies in human serum may react with immunoglobulin in the reagent or sample, and interfere with immunoassay in vitro. More clinical or diagnostic information is needed to confirm disease status of patients.

Some patients have frequent contact with animals, or have been treated or diagnosed with mouse monoclonal antibodies. They may have generated heterophilic antibodies. For example, some patients under monoclonal antibody treatment may have human anti-mouse antibodies (HAMA) in blood circulation, leading to false positive or false negative results. Anti-interference components are added to this reagent formulation to minimize the impact of HAMA, but the problem may not be totally eliminated, and some sample testing may still be impacted. More clinical and diagnostic information is needed to make a solid conclusion.

For RF at a concentration of less than 1500 IU/mL, and HAMA at a concentration of less than 120 ng/mL, measurement error by the interference is within ±10%.

**[Property and Performance]**

**1 Limit of Blank**

LoB ≤ 0.05 ng/mL.

**2 Limit of Detection**

LoD ≤ 0.1 ng/mL.

**3 Accuracy**

Accuracy should meet at least one of the following criteria:

a) Take International reference material which can be used to prepare the reference samples for routine evaluation. The relative error between measured result and target concentration is less than ±10.0 %.

b）Test the accuracy reference samples at two concentration levels multiple times. The relative deviation between the measurement result and the target value must not exceed 10.0%.

c) Spike PROG of a known concentration into real samples at different PROG levels. Spiked recovery should be 100±15%.

**4 Linearity**

Test PROG samples with concentration in the range of 0.1~50 ng/mL, the linearity correlation coefficient r ≥ 0.9900.

**5 Repeatability**

Coefficient of variation (CV) for the test results of low (2.5±1.8 ng/mL) and high (20±6 ng/mL) corporate reference sample is less than 8.0 %.

**6 Lot-to-lot Variation**

Coefficient of variation (CV) for the test results of low (2.5±1.8 ng/mL) and high (20±6 ng/mL) corporate reference sample with three batches of reagent is less than 10.0 %.

**7 Accuracy of Calibrator Value Assignment**

Use primary calibrators with assigned values from higher level measurement procedure, calibrate the immunoassay analyzer, and use the same lot of reagent to measure the value of each product calibrator. The measured value of Calibrator C1 and C2 has a relative deviation within ±10.0 % from its assigned value.

**8 Homogeneity of Calibrators**

**8.1 Within-vial Homogeneity**

Within-vial homogeneity of Calibrator C1 or C2 is represented with coefficient of variation, and CV≤8.0 %.

**8.2 Between-vial Homogeneity**

Between-vial homogeneity of calibrator C1 or C2 is represented with coefficient of variation, and CV≤5.0 %.

**[Attention Notes]**

1 It is for in-vitro diagnosis only.

2 It can only be used by professionals.

3 Never use expired reagent kit.

4 Never mix components from different kits, or from different reagent lots.

5 Do not put the reagent cartridges upside down.

6 Measurement of PROG in a sample using different detection systems may yield different results, due to the difference in test methods, assay specificity, and factors of interference. The measured values from different systems should not be directly compared to avoid inappropriate clinical interpretation.

7 Strictly follow the protocol in the package insert, and operate according to the lab guidelines.

8 The test results can only be used for clinical reference. Clinical diagnosis of patients should take symptoms, body sign, disease history, other laboratory test results, and response to treatment for comprehensive assessment.

9 User should wear gloves and lab coat. Rinse with water if the skin is in contact with the reagent. Flush eyes with copious of water if eyes are in touch with the reagent, and see a doctor immediately.

10 Take all samples and reaction waste as potential biohazards. All waste must be handled following the local government regulation.

11 This product is a single-use cartridge. Reagent cartridge should be put back into refrigerator and stored at 2~8°C if they are not opened within the same day.

**[Interpretation of Signs]**

| | | | |
|---|---|---|---|
|  | Temperature limit. |  | Date of manufacturing |
|  | In-vitro diagnostic medical device |  | Catalogue number |
|  | Batch Code |  | Consult instruction for use |
|  | Use-by Date |  | Authorized representative in the European Community |
|  | This way up |  | CE marking of conformity |
|  | Manufacturer |  | Unique device identifier |
|  | Biological risks | | |

**[References]**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**[Basic Information]**


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**[Issued on]**

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