Urine Beta hCG (pregnancy) testing with DXpress Reader

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LOCATION OF COPIES	1. PoCT Office 2. Q-PULSE 3. Appendix on wall A+E

CONTENTS

1 SCOPE AND PURPOSE

Detection of raised human beta chorionic gonadotropin to diagnose pregnancy, missed abortion and ectopic pregnancy.

2 RESPONSIBILITY

The head of department has overall responsibility for the performance of this assay.
Routine running, staffing and Quality Assurance are the responsibility of a senior member of staff under the direction of the head of department.
Review and updating of the Standard Operating procedure is the responsibility of the Point of Care Testing Manager with reference to current documentation.

3 REFERENCES

1. Braunstein, G.D., Rasor, J., Adler, D., Danzer, H., and Wade, M.E. Serum Human Chorionic Gonadotropin Levels Throughout Normal Pregnancy, Am. J. Obstet. Gynecol. 1976; 126:678.
2. Krieg, A.F. Pregnancy Tests and Evaluation of Placental Function in: Clinical Diagnosis and Management by Laboratory Methods, 16th ed., Henry, J.B. (ed.) W.B. Saunders Co., Philadelphia, pp. 680, 1979.
3. See references on pack insert Q-Pulse POC-Ext-16.

4 DEFINITIONS

β-HCG	Beta Human Chorionic Gonadatropin, the hormone measured as an indicator of pregnancy.
PoCT	Point of care Testing, pathology investigations performed outside the laboratory setting.
QC	Quality Control, materials or processes used to check system performance.
EQA	External Quality Assurance, materials/processes used to check system performance that are supplied by an external source.

5 RELATED DOCUMENTS

Medical Devices Policy.
Infection Control Policy.
POC-EXT-22 Extract from training manual see appendix A.
POC-EXT-16 BioSign hCG One Step Pregnancy Urine Test REF BSP -121 kit insert see appendix B.

6 ACTIONS AND METHODS

6.1 Principle of test

High sensitivity testing based on an immunochemical sandwich assay, relying on the recognition and formation of specific antibody – hCG - antibody+dye complexes on a porous carrier. The membrane is coated with mouse anti-hCG in the Test Band region and goat anti-mouse in the Control Band region, and a monoclonal anti-hCG/colloidal gold conjugate is coated in the sample application region. When urine is added to the sample well it migrates along the membrane mixing with and carrying the coloured gold-conjugate. If the urine contains >25 mIU/mL of hCG then a detectable line will form in the Test Band region. If the level of hCG in the sample is less than 25 mIU/mL then no line will be detected, but in both cases a line must be detected at the Control Band region to demonstrate that test function is satisfactory. The DXpress reader uses image analysis to “read” the test cassette and compares the colour intensity of the lines against calibration values held in its memory and derives a qualitative result.

6.2 Personnel to do the task / level of training required

Staff should only undertake the procedure if they have had the relevant training.

6.3 Specimen requirements

Volume Required: 3 drops fresh urine. Early morning samples are best as they are more concentrated, very dilute urines should be avoided.
Storage: Samples may be stored in a container, without additive, refrigerated at 2--8°C for 2 days or longer frozen. N.B. Samples must be brought to room temperature and mixed before testing.

6.4 Equipment

DXpress cassette reader (LSR 2000P)
BioSign hCG One Step Pregnancy Urine Test (web basket BSP 12235)
Blank calibrator (R2810)

6.5 Materials/Reagents

Printer paper (TPR24) or Labels (SPR24).

6.6 Quality Control

Status Control kit 135-100A (Positive and Negative)
External WEQAS scheme.
System and cassette self checks.
Internal quality controls will be run periodically.
External quality controls are circulated bi monthly and should be run by user as patient tests.
System calibration will be performed by PoCT staff weekly.

Regular system checks need to be performed by selecting the following:

Main menu> Option 2 “Run QC” > Option 1”Self Check”.

6.7 Method/Procedure

The test device must not be used if the foil pouch containing it is damaged in any way e.g. there is a tear in it.
Once the pouch is opened the test must be used within 5-10 minutes or discarded and another opened.

Test Protocol

See attached manufacturer instruction in Appendix A if the reader should fail tests can be performed manually as in Appendix B.
If uncertain of the result repeat the test ensuring that correct timing and sample application have been used in a well lit environment. If possible get another person to view the result. If still inconclusive repeat the test 48hrs later ensuring a reasonably concentrated sample is used. If an urgent result is required, contact the Biochemistry Laboratory for advice.
Refer to kit insert attached for further details.

6.8 Result Reporting

Results must be entered clearly into the notes as positive or negative and the date, time and person performing the test must also be recorded. As stated in the pack insert the result must not be read after 5mins.

6.9 Reference Ranges

See below.

6.10 Guide to interpretation

In normal pregnancy, hCG can be detected 7-10 days after conception. Usually, the test can be used as early as the first day of a missed period. If the menstrual cycle length is irregular, the test time can be based on the longest cycle length that occurred in the past few months. If a negative result is obtained and pregnancy is still suspected, the test can be repeated in 2-4 days.
In normal pregnancies hCG will reach 20 iu/L in 4-5 days (visible as a weak positive). However the detection of hCG at this level does not necessarily indicate a viable pregnancy as implantations can spontaneously abort.
An ectopic pregnancy will show a much slower rise or even plateau with hCG values lower than for a comparable stage of normal pregnancy. A fall in concentration will suggest a failing pregnancy or miscarriage. The time post miscarriage before the levels become undetectable will depend on the peak level of hCG reached.
Raised levels of hCG are also present in other conditions e.g. hydatidiform moles/choriocarcinoma.
Current practice has brought about the requesting of quantitative serum hCG. These are currently available on request from Biochemistry but are only

routinely available for ectopic pregnancy screening (when abdominal ultra-sound scans are negative) with two serum samples 48h apart. The assay of a sample urgently is generally not indicated but can be provided after discussion with Biochemistry.

6.11 WEQAS Scheme

Upon receipt of the External Quality Controls, please treat as a patient urine sample and perform a pregnancy test on each sample.
Record the results on the sheet provided ensuring the results are noted against the correct sample.

Once completed return the form to PoCT, Pathology, Level One, NDDH.

The results are processed by a national reference centre and participating departments will be notified of results.

7 HEALTH AND SAFETY / COSHH

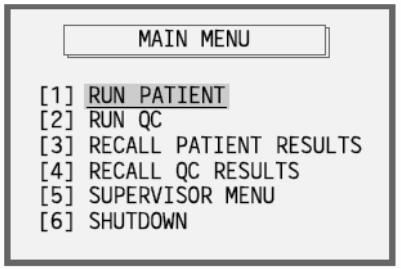
Some components may contain human source material and/or other potentially hazardous ingredients that necessitate certain precautions:

Handle all components and all patient samples as recommended for any potentially infectious human serum or blood specimen in the HHS Publication No. (CDC) 93-8395, *Biosafety* in Microbiological and Biomedical Laboratories, U.S. Government Printing Office; Washington, DC, 1993, pages 16–18. Follow Universal Precautions when handling patient specimens as detailed by the Infection Control Manual.

Use disposable gloves. Wipe up spills promptly and decontaminate affected surfaces. Avoid generation of aerosols. Follow appropriate waste handling regulations applicable to your area (see Safety Code of Practice section 22).

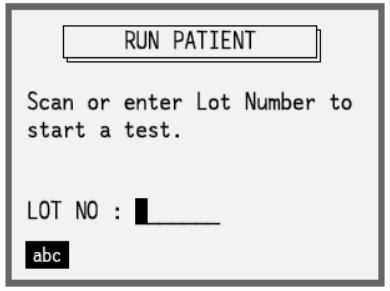
8.0 APPENDIX A

1



SELECT **[1] RUN PATIENT.**

2



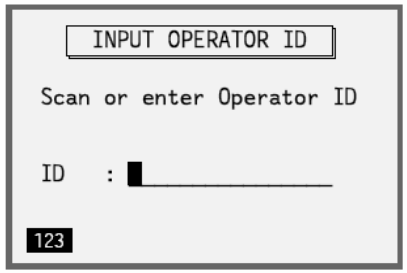
Scan the Lot Number barcode on the box or pouch (if available) or enter the Lot Number using the keypad.

3

Confirm the Product Name and Lot Number displayed on the screen. *SELECT* **OK** to go to the next step or **CANCEL** to re-enter the Lot Number.

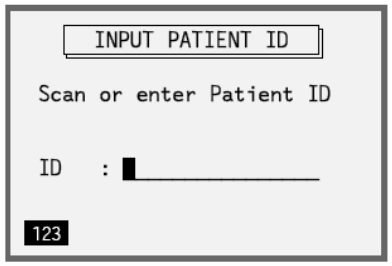
The reader will automatically check whether this Lot Number and associated calibration profile exist in the reader database.

4



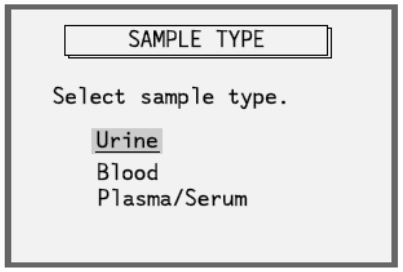
SCAN or *ENTER* the Operator ID (up to 16 characters).

5



SCAN or *ENTER* the Patient ID(s) (up to 16 characters).

6

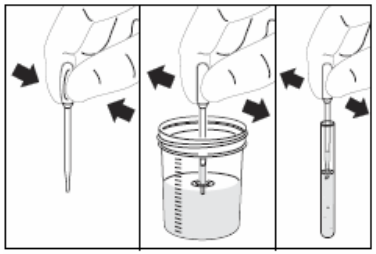


With Urine highlighted, as illustrated, press ENTER to select it

7 Take a test cassette out of the box and check if the foil pouch containing it is damaged in any way, if there is any sign of damage discard it and use another test cassette. Tear open the foil pouch and follow the steps below.
Once the pouch is opened the test must be used within 5-10 minutes or discarded and another opened.

8

Draw Sample Into Dropper

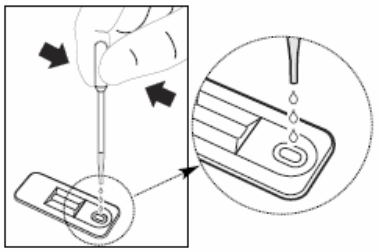


- Draw sample into dropper by first squeezing dropper bulb to create a vacuum, then dipping dropper end into the sample and then releasing dropper bulb.

NOTE: Avoid introducing air bubbles into dropper.

9

Add Sample to Test Cassette

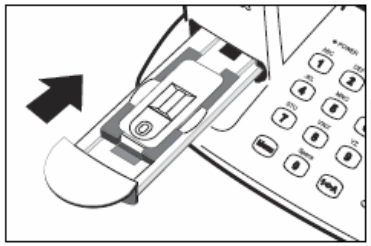


- Holding dropper vertically, squeeze the dropper bulb to dispense 3 full drops into test sample well.

NOTE: Do not touch sample well or test cassette with the tip of dropper.

10

Insert Test Cassette Into Reader

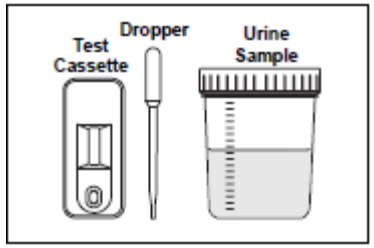
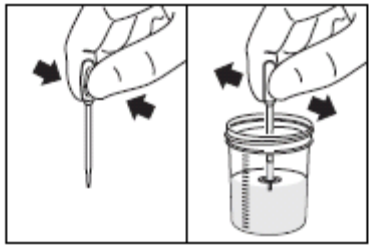
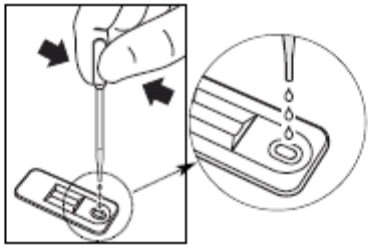
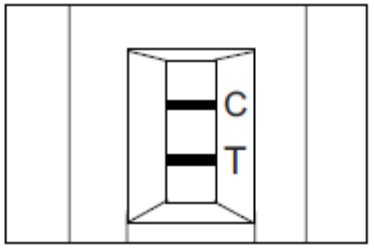


- IMMEDIATELY place test cassette into Reader tray and then close tray to start countdown (incubation) timer.

11 The result will be displayed on screen and printed on the tear off label.
Remove the used test cassette and dispose of it in the appropriate bin for biologically contaminated waste.
Ensure the cassette tray is shut to prevent damage/contamination.

8.1 APPENDIX B (MANUAL PROCEDURE)

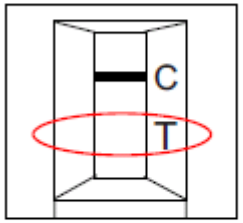
Test Procedure - BioSign® hCG Urine Test

STEP 1	STEP 2	STEP 3	STEP 4
Collect Sample & Prepare Parts	Draw Sample Into Dropper	Add Sample to Test Cassette	Wait 3 Minutes & Read Result
			
▸ Collect urine sample. ▸ Check expiry date on test cassette pouch. ▸ Tear open pouch and remove test cassette and dropper. ▸ Write patient ID on test cassette and place on a flat surface.	▸ Draw sample into dropper by first squeezing dropper bulb to create a vacuum, then dipping dropper end into the sample and then releasing dropper bulb. NOTE: Avoid introducing air bubbles into dropper.	▸ Holding dropper vertically, squeeze the dropper bulb to dispense 3 full drops into test sample well. NOTE: Do not touch sample well or test cassette with the tip of dropper.	▸ Read result at 3-5 minutes. ▸ DO NOT read result after 5 minutes.

Reading of Results - BioSign® hCG Urine Test

Result Key | **Control** Line ⇨ Valid | No Line ⇨ Invalid | **Test** No Line ⇨ Negative | Line (clearly distinguishable) ⇨ Positive

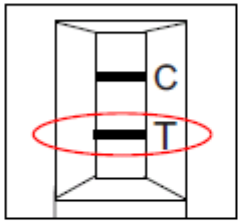
NEGATIVE RESULT



C [Control line]:
- VALID

T [Test line]:
- NEGATIVE

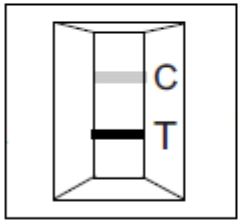
POSITIVE RESULT



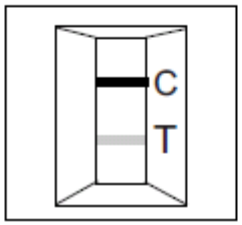
C [Control line]:
- VALID

T [Test line]:
- POSITIVE

OR

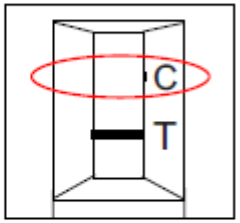


OR



To be interpreted as positive, the pink-purple Test line should be clearly distinguishable from the background colour of the membrane.
In strong positive tests, the colour intensity of the Control line may be much lighter than that of the Test line.

INVALID RESULT



C [Control line]:
- INVALID

T [Test line]:
- INVALID

8.2 APPENDIX C

P-51103

BioSign® hCG

Urine Pregnancy Test

For Professional *In Vitro* Diagnostic Use Only

Rapid Immunoassay for the Qualitative Detection of Human Chorionic Gonadotropin in Urine with DXpress™ Reader

For the Early Detection of Pregnancy

PBM

CDC Analyte Identifier Code: 9642
CDC Test System Identifier Code: 49200

Stock No.	BSP-121	35 Test Kit
	BSP-121-10	10 Test Kit

Intended Use

BioSign® hCG Test is a simple immunoassay for the qualitative detection of human chorionic gonadotropin (hCG) in urine for the early confirmation of pregnancy. This test is intended to be used with the DXpress™ Reader.

Summary and Explanation

Human chorionic gonadotropin (hCG) is a glycoprotein hormone produced by the placental trophoblastic cells shortly after the implantation of fertilized ovum in the uterine wall.[1-4] The primary function of hCG is to maintain the corpus luteum during early pregnancy. The appearance of hCG in urine soon after conception and its rapid rise in concentration make it an excellent marker for confirmation of pregnancy. The hormone can be detected in urine as early as 7 to 10 days after conception.[1-4] The concentration of hCG continues to rise rapidly, frequently exceeding 100 mIU/mL by the first missed menstrual period and peaking in the 100,000–200,000 mIU/mL range by 10 to 12 weeks into pregnancy. The hormone is comprised of two non-covalently bound dissimilar subunits containing approximately 30% carbohydrate by weight.[5] The alpha subunit is structurally similar to other human pituitary glycoprotein hormones, whereas the beta (ß) subunit confers unique biological and immunological specificity to the molecule.[6,7]

Principle

The **BioSign® hCG Test** is a rapid urine test for detecting hCG qualitatively. The test employs a solid-phase, chromatographic immunoassay technology to detect elevated levels of hCG in urine with a high degree of sensitivity. In the test procedure, sample is added to the sample well with a transfer pipette. If hCG is present in the specimen, it will react with the conjugate dye, which binds to the antibody on the membrane to generate a colored line. The DXpress™ Reader interprets the test result automatically by comparing the intensity of the test line to the preset cutoff value. The hCG levels greater than or equal to 25 mIU/mL are reported as positive. Samples containing less than 25 mIU/mL are reported as either negative or borderline.

Reagents

The **BioSign® hCG Test** kit contains complete reagent components and materials to perform the test.

Materials Provided

- **BioSign® hCG Test:** Each device contains mouse monoclonal and goat anti-hCG antibodies
- Disposable dropper
- Package insert

Materials Required but Not Provided

- Specimen cup
- DXpress™ Reader

Materials Recommended but Not Provided

- Timer
- External positive and negative controls

Precautions

- For *in vitro* diagnostic use only.
- Do not interchange materials from different product lots and do not use beyond the expiration date.
- The test device should remain in its sealed pouch until ready for use.

Storage and Stability

BioSign® hCG Test kit is to be stored at 2°C to 30°C (35°F to 86°F) in the sealed pouch.

Specimen Collection and Preparation

- Approximately 110 µL of sample is required for each test.
- Specimens containing particulate matter may give inconsistent test results. Such specimens should be clarified by centrifugation prior to assaying.
- Frozen specimens must be completely thawed, thoroughly mixed, and brought to room temperature prior to testing by allowing the specimens to stand at room temperature for at least 30 minutes.
- For optimal early detection of pregnancy, a first morning urine specimen is preferred since it generally contains the highest concentration of hCG of the day. However, randomly collected urine specimens may be used.
- Collect the urine specimen in a clean glass or plastic cup.

Specimen Storage

- If testing will not be performed immediately, the specimens should be refrigerated (2°C to 8°C) for up to 72 hours prior to assay.
- For prolonged storage, specimens should be frozen and stored below -20°C. Frozen specimens must be completely thawed, thoroughly mixed before using. Avoid repeated freezing and thawing.
- If specimens are to be shipped, they should be packed in compliance with Federal regulations covering the transportation of etiologic agents.

Procedure

Test Procedure Summary

The procedure consists of adding the specimen to the sample well in the device, inserting the device into the DXpress™ Reader and following the instructions to get the result.

Procedural Notes

- Allow the dropper to fill with sample without air bubbles.
- Handle all specimens as if capable of transmitting disease.
- After testing, dispose of the **BioSign®** device, and the specimen dispenser following good laboratory practices. Consider each material that comes in contact with specimen to be potentially infectious.

Using Dxpress™ Reader

For complete instructions, including installation and start up, refer to the DXpress™ Reader User Manual. Operators must consult the DXpress™ Reader User Manual prior to use and become familiar with the processes and quality control procedures.

1

Performing Self Check

Each time the DXpress™ Reader is turned on, Self Check is automatically performed and the operator may then proceed to Calibration QC. If the DXpress™ Reader is left on or in power save mode, the operator should perform Self Check daily, as follows:

From the Main Menu, select:	[2] RUN QC
Then select	[1] SELF CHECK

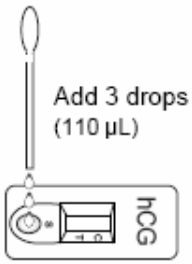
Self Check takes about 15 seconds. PASS or FAIL results will be displayed/printed when testing is completed. All Self Check items should pass before testing patient samples.

Note: Perform Calibration QC in accordance with your laboratory procedures. Consult the DXpress™ Reader User Manual for more information.

Testing Patient Samples

Patient samples may be tested using the DXpress™ Reader Scheduler mode, as described below. To use other modes (batch mode or read-now mode) consult the DXpress™ Reader User Manual.

1. Open the pouch and remove the test device.
- Write the patient ID on the test device.
- Place the test device on a level surface.
2. Enter test information in the DXpress™ Reader:
- From the Main Menu, select [1] RUN PATIENT.
- Scan lot number barcode from the box or pouch.
- Confirm test device information and lot number as displayed on the screen and press ENTER.
- Scan or enter the Operator ID.
- Scan or enter the Patient ID.
- From the Incubation Time window, select SCHEDULER.
3. Add patient sample to the test device by holding the dropper in a vertical position and adding 3 drops of sample into the sample well. Press ENTER on the Dxpress™ Reader.



4. Place the test device in the Reader tray, and close the tray.
5. After 5 minutes of incubation the DXpress™ Reader will automatically display the results on the screen.
- Results may be printed by pressing PRINT button.
- At this point the test device may be removed and appropriately discarded.

Interpretation of Results

Positive

The instrument will automatically determine the result as positive if the test line intensity is greater than or equal to 25 mIU hCG/mL and confirm that the control line intensity meets the minimum requirement.

Negative

The instrument will automatically determine the result as negative if the test line intensity is less than 25 mIU hCG/mL and confirm that the control line is present (valid test).

Borderline Results

Samples reported as borderline are considered indeterminate and the operator is advised to repeat the test with a new specimen obtained 48-72 hours later.

Invalid

The instrument will automatically determine if a procedural error has occurred by confirming that the control line is not present (invalid test).

If the result is invalid, the sample should be retested with a new device. If the problem persists, contact your local distributor of PBM.

Limitations

- The result cannot be interpreted visually. The result can only be read by the DXpress™ Reader.
- An extremely low concentration of hCG during the early stage of pregnancy can give a negative result. In this case, testing of another specimen obtained at least 48 hours later is recommended.
- A false negative result could be possible in case of ectopic pregnancy due to the fact that the concentration of hCG level tends to be lower than those with a normal pregnancy.[11]
- Low levels of hCG have been reported in non-pregnant females with no history of ectopic pregnancy, trophoblastic disease or germ-cell tumors.[12] In the case of Borderline test results testing of another specimen obtained at least 48 hours later is recommended.
- The hCG level may remain detectable for several weeks after normal delivery, delivery by caesarean section, spontaneous abortion, or therapeutic abortion.[14]
- The test is highly sensitive, and specimens which test positive during the initial days after conception may later be negative due to natural termination of the pregnancy. Natural termination occurs in 22% of clinically unrecognized pregnancies and 31% of pregnancies overall.[15] Subsequent testing of a new urine sample after an additional 48 hours is recommended in order to confirm that the hCG level is rising as indicated in a normal pregnancy.
- Elevated hCG levels have been reported in patients with both gestational and nongestational trophoblastic diseases.[8,9,10] The hCG of trophoblastic neoplasms is similar to that found in pregnancy, so these conditions, including choriocarcinoma and hydatidiform mole, should be ruled out before pregnancy is diagnosed.
- The physician should evaluate data obtained with this kit in light of other clinical information.
- Samples which contain excessive bacterial contamination or which have been subjected to repeated freezing and thawing should not be used because such specimens can give spurious results.
- Degradation of hCG in sample may occur by a certain protease during storage even at 4° C and give a negative test result.
- In rare occasions, persistent low levels of hCG present in men and in non-pregnant women (concentrations 3 to 100 mIU/mL) may result in positive results.[11, 13]

User Quality Control

Internal Control: Each **BioSign® hCG Test** device has a built-in control. The Control line is an internal positive procedural control. A distinct reddish-purple Control line should appear at the C position, indicating an adequate sample volume is used, the sample and reagent are wicking on the membrane, and the reagents at the Control line and the conjugate-color indicator are reactive. In addition, the clearing background in the Result window, by providing a distinct readable result, may be considered an internal negative procedural control. If background color appears in the Result window, which interferes with the result interpretation of the reader, then the result is invalid. If the problem persists, contact PBM for technical assistance.

External Control: External controls may also be used to assure that the reagents are working properly and that the assay procedure is followed correctly. It is recommended that a control be tested before using a new lot or a new shipment of kits as good laboratory testing practice and that users follow federal, state, and local guidelines for quality control requirements. For information on how to obtain controls, contact PBM Technical Services.

Expected Values

BioSign® hCG Test is capable of detecting hCG level of 25 mIU/mL (calibrated against the WHO 4th International Standard). HCG levels in normal early pregnant women vary and hCG levels often exceed 100 mIU/mL by the first day of the missed menstrual period.' The test is usually capable of detecting hCG by the first day of the missed menstrual period.

Performance Characteristics

Comparison Study

A total of 65 clinical samples were studied. These specimens were assayed with **BioSign® hCG Test** and a predicate device according to the respective test's protocol. The summary of the results is shown in Table 1.

Table 1. BioSign® vs. Predicate Device

		BioSign® hCG			
		Positive	Borderline	Negative	Total
Predicate Device	Positive	37	1	0	38
	Negative	0	1	26	27
	Total	37	2	26	65

Two samples gave discrepant results between **BioSign® hCG** and the predicate devices. These two samples contained hCG, but the amount of hCG present in these samples was less than 25mIU/mL. The **BioSign® hCG** gave borderline (indeterminate) results for these two samples, while the predicate device gave 1 positive and 1 negative result for these two samples.

All discrepant samples had less than 25 mIU/mL hCG. **BioSign® hCG Test** gave correct results (borderline or negative) for all these samples.

Sensitivity

To evaluate analytical sensitivity of **BioSign® hCG Test**, the following experiment was performed.

Pooled negative from non-pregnant people was spiked with hCG at several levels. Each level was tested 20 times with two lots. The result is summarized in Table 2.

This data supports that **BioSign® hCG Test** detects hCG concentrations equal to or greater than 25 mIU/mL (calibrated to the WHO 4th International Standard).

Table 2. BioSign® hCG Sensitivity Study

hCG (mIU/mL)	Percent Positive (N)
0	0
3	0
5	0
10	0
15	30 (6)
20	80 (16)
25	100 (20)
40	100 (20)

Precision Study

The precision of **BioSign® hCG Test** was determined by carrying out the test with hCG spiked into pooled negative samples. Four levels of hCG concentration were tested for three days with 2 lots and three DXpress readers. There were no significant differences between readers, between days or between lots. Table 3 shows the precision data combining all repeated tests.

Table 3. Summary of Precision Study Data

hCG Conc. (mIU/mL)	Total No. Tested	No. of Positive	No. of Borderline	No. of Negative	% Correct Results
0	180	0	0	180	100
5	180	0	3	177	98.3
25	180	179	1	0	99.4
40	180	180	0	0	100

Physicians' Office Laboratory Evaluation

Reproducibility of **BioSign® hCG** test results was evaluated at three physicians' office laboratories using a total of 120 blind control samples. Each panel consisted of five negative (–) samples, five at 5 mIU/mL, five at 25 mIU/mL, and five at 100 mIU/mL hCG. The results obtained at each site agreed 100% with expected results.

Specificity

The assay is free from interference with other commonly known homologous hormones when tested at the levels specified below.

Homologous Hormones	
hFSH	1000 mIU/mL
hLH	300 mIU/mL
hTSH	1000 µIU/mL

Interfering Substances

Potentially interfering substances were prepared at the following concentrations containing either 0 or 25 mIU/mL hCG. These samples were tested with the **BioSign® hCG Test**. No interference was found (Table 4) at these concentration.

Table 4. Interfering Substances and Concentrations Tested

Substance Added	Concentration Added
Acetaminophen	20 mg/dL
Acetylsalicylic Acid	20 mg/dL
Ampicillin	20 mg/dL
Ascorbic Acid	20 mg/dL
Atropine	20 mg/dL
Caffeine	20 mg/dL
Gentisic Acid	20 mg/dL

Phenothiazine	20 mg/dL
Phenylpropanolamine	20 mg/dL
Salicylic Acid	20 mg/dL
Tetracycline	20 mg/dL
Bilirubin	1 mg/dL
Glucose	2000 mg/dL
Hemoglobin	1 mg/dL
Ketones	100 mg/dL

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Symbols Key

	Manufactured by
CE	CE Mark
EC REP	Authorized Representative
IVD	*In Vitro* Diagnostic Medical Device
REF	Catalog Number
	Consult Instructions for Use
LOT	Batch Code
EXP	"Use By" date in year-month-day format
	Temperature Limitation
n	Contains sufficient for <n> tests
	Do not reuse
CONT	Contents
DEV	Test Device
PIP	Transfer Pipette
IFU	Instructions for Use
TEST PREG	Pregnancy Test

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