ARCHITECT Prolactin

REF 7K76-25
REF 7K76-20
REF 7K76-35
REF 7K76-30

en
Prolactin
7K76
G6-5314/R06
B7K760

Read Highlighted Changes: Revised January 2016.

Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

NAME

ARCHITECT Prolactin

INTENDED USE

The ARCHITECT Prolactin assay is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of prolactin in human serum and plasma.

SUMMARY AND EXPLANATION OF THE TEST

Human prolactin (hPRL) is a single chain polypeptide of 199 amino acids and a molecular weight of approximately 23,000 daltons. Its existence as a distinct chemical entity, separate from growth hormone, was established through a series of studies between 1965 and 1971[1, 2] Prolactin is produced by the anterior pituitary and its secretion is regulated physiologically by inhibitory[3] and releasing[4] factors of the hypothalamus. Prolactin appears in the blood promptly after administration of thyrotropin-releasing hormone (TRH).[4, 5] The major physiologic action of prolactin is the initiation and maintenance of lactation in women.

Hyperprolactinemia has been established as a common cause of infertility and gonadal disorders in men and women. Prolactin has been shown to inhibit the secretion of ovarian steroids[6, 7] and to interfere with follicle maturation[7] and the secretion of LH and FSH[8] in the human female. Measurement of elevated serum prolactin levels may provide the first quantitative evidence of pituitary dysfunction.[9] Quantitation of prolactin levels is also of interest in the evaluation and management of patients with amenorrhea and galactorrhea.[10]

Various factors other than disease states have been found to influence prolactin levels. Factors which increase prolactin concentrations include: pregnancy, breast stimulation, stress, coitus, administration of estrogens, progesterone, androgens, some psychotropic and antihypertensive drugs, and TRH.[10, 11]Factors which decrease prolactin concentrations include the administration of L-dopa and bromocriptine.[10, 11]

The ARCHITECT Prolactin assay is to be used as an aid in the diagnosis of male and female infertility and pituitary dysfunction, monitoring of male and female gonadal disorders and management of amenorrhea and galactorrhea.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT Prolactin assay is a two-step immunoassay to determine the presence of prolactin in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex.

1. Sample and anti-prolactin (mouse, monoclonal) coated paramagnetic microparticles are combined. The prolactin present in the sample binds to the anti-prolactin (mouse, monoclonal) coated microparticles.
2. After washing, anti-prolactin (mouse, monoclonal) acridinium-labeled conjugate is added to create a reaction mixture.
3. Following another wash cycle, Pre-Trigger and Trigger Solutions are added to the reaction mixture.
4. The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of prolactin in the sample and the RLUs detected by the ARCHITECT iSystem optics.

For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.

REAGENTS

Kit Contents

ARCHITECT Prolactin 7K76

NOTE: Some kit sizes are not available in all countries or for use on all ARCHITECT iSystems. Please contact your local distributor.

REF	7K76-25	7K76-20	7K76-35	7K76-30
Σ	100	400	500	2000
MICROPARTICLES	1 x 6.6 mL	4 x 6.6 mL	1 x 27.0 mL	4 x 27.0 mL
CONJUGATE	1 x 5.9 mL	4 x 5.9 mL	1 x 26.3 mL	4 x 26.3 mL

MICROPARTICLES Anti-prolactin (mouse, monoclonal) coated Microparticles in TRIS buffer with protein (bovine and murine) stabilizers. Minimum concentration: 0.1% solids. Preservative: antimicrobial agent.

CONJUGATE Anti-prolactin (mouse, monoclonal) acridinium-labeled Conjugate in phosphate buffer with protein (piscine and bovine) stabilizers. Minimum concentration: 0.05 µg/mL. Preservative: ProClin.

Other Reagents

MULTI-ASSAY MANUAL DILUENT 1 x 100 mL ARCHITECT Multi-Assay Manual Diluent, REF 7D82-50, containing phosphate buffered saline solution. Preservative: antimicrobial agent.

PRE-TRIGGER SOLUTION ARCHITECT Pre-Trigger Solution containing 1.32% (w/v) hydrogen peroxide.

TRIGGER SOLUTION ARCHITECT Trigger Solution containing 0.35 N sodium hydroxide.

WASH BUFFER ARCHITECT Wash Buffer containing phosphate buffered saline solution. Preservatives: antimicrobial agents.

NOTE: Bottle and volume varies based on order.

Warnings and Precautions

- IVD
- For *In Vitro* Diagnostic Use

Safety Precautions

CAUTION: This product requires the handling of human specimens. It is recommended that all human-sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens. Biosafety Level 2 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.[12-15]

The following warnings and precautions apply to: CONJUGATE	
	
WARNING	Contains methylisothiazolones.
H317	May cause an allergic skin reaction.
Prevention	
P261	Avoid breathing mist / vapors / spray.
P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P302+P352	IF ON SKIN: Wash with plenty of water.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

Safety Data Sheets are available at www.abbottdiagnostics.com or contact your local representative.

For a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Reagent Handling

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a kit or between kits.**
- Before loading the reagent kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. For microparticle mixing instructions, refer to the **PROCEDURE, Assay Procedure** section of this package insert.
- **Septums MUST be used to prevent reagent evaporation and contamination and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in this package insert.**
  - To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.
  - Once a septum has been placed on an open reagent bottle, **do not invert the bottle** as this will result in reagent leakage and may compromise assay results.
  - Over time, residual liquids may dry on the septum surface. These are typically dried salts and have no effect on assay efficacy.

For a detailed discussion of handling precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 7.

Reagent Storage

When stored and handled as directed, reagents are stable until the expiration date.

	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
Unopened/ Opened*	2-8˚C	Until expiration date	May be used immediately after removal from 2-8˚C storage. Store in upright position.
On board	System temperature	30 days	Discard after 30 days. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.

* Reagents may be stored on or off the ARCHITECT iSystem. If reagents are removed from the system, store them at 2-8˚C (with septums and replacement caps) in an upright position. For reagents stored off the system, it is recommended that they be stored in their original trays and boxes to ensure they remain upright. **If the microparticle bottle does not remain upright (with a septum installed) while in refrigerated storage off the system, the reagent kit must be discarded.** For information on unloading reagents, refer to the ARCHITECT System Operations Manual, Section 5.

Indications of Reagent Deterioration

When a control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results are invalid, and samples must be retested. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

The ARCHITECT Prolactin assay file must be installed on the ARCHITECT iSystem from an ARCHITECT iSystem Assay CD-ROM prior to performing the assay.

For detailed information on assay file installation and viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.

For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.

For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.

Alternate Result Units

Edit assay parameter "Result concentration units" to select an alternate unit.

Conversion formula:

(Concentration in Default result unit) x (Conversion factor) = (Concentration in Alternate result unit)

Default result unit	Conversion factor	Alternate result unit
ng/mL	21	mIU/L

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

Validated specimen types to be used with this assay:

Specimen Types	Collection Tubes
Human Serum	Serum
	Serum separator tubes
Human Plasma	Sodium heparin
	Lithium heparin
	Potassium EDTA

- Other anticoagulants have not been validated for use with the ARCHITECT Prolactin assay.
- The instrument does not provide the capability to verify specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the assay.

Specimen Conditions

- For optimal results, serum and plasma specimens should be free of fibrin, red blood cells or other particulate matter.
- Ensure that complete clot formation in serum specimens has taken place prior to centrifugation. Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy may exhibit increased clotting time. If the specimen is centrifuged before a complete clot forms, the presence of fibrin may cause erroneous results.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for specimen collection tubes.
- Specimens must be mixed THOROUGHLY after thawing, by LOW speed vortexing or by gently inverting, and centrifuged prior to use to remove red blood cells or particulate matter to ensure consistency in the results.
- Inspect all specimens for bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

Specimen Storage

Specimen Type	Storage Temperature	Maximum Storage Time
Serum/Plasma	2-8°C	≤ 7 days

If testing will be delayed more than 24 hours, remove serum or plasma from the clot, serum separator or red blood cells.

If testing will be delayed more than 7 days, specimens should be frozen at -10°C or colder. Specimens stored frozen at -10°C or colder for 12 months showed no performance differences.

Avoid multiple freeze/thaw cycles.

Specimen Shipping

- Package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- Do not exceed the storage limitations listed above.

PROCEDURE

Materials Provided

7K76 ARCHITECT Prolactin Reagent Kit

Materials Required but not Provided

- ARCHITECT Prolactin Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 7K76-01 ARCHITECT Prolactin Calibrators
- 7K76-10 ARCHITECT Prolactin Controls
- 7D82-50 ARCHITECT Multi-Assay Manual Diluent
- ARCHITECT Pre-Trigger Solution
- ARCHITECT Trigger Solution
- ARCHITECT Wash Buffer
- ARCHITECT Reaction Vessels
- ARCHITECT Sample Cups
- ARCHITECT Septum
- ARCHITECT Replacement Caps
- Pipettes or pipette tips (optional) to deliver the volumes specified on the patient or control order screen.

For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.

Assay Procedure

- Before loading the reagent kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. After the first time the microparticles have been loaded, no further mixing is required.
  - **Invert the microparticle bottle 30 times.**
  - Visually inspect the bottle to ensure microparticles are resuspended. If microparticles are still adhered to the bottle, continue to invert the bottle until the microparticles have been completely resuspended.
  - **If the microparticles do not resuspend, DO NOT USE. Contact your local Abbott representative.**
  - Once the microparticles have been resuspended, place a septum on the bottle. For instructions about placing septums on bottles, refer to the **Reagent Handling** section of this package insert.
- Load the reagent kit on the ARCHITECT iSystem.
  - Verify that all necessary reagents are present.
  - Ensure that septums are present on all reagent bottles.
- Order calibration, if necessary.
  - For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.
- Order tests.
  - For information on ordering patient specimens and controls and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- Minimum sample cup volume is calculated by the system and printed on the Orderlist report. To minimize the effects of evaporation, verify adequate sample cup volume is present prior to running the test.

  Maximum number of replicates sampled from the same sample cup: 10
  - Priority:

    Sample volume for first test: 80 µL

    Sample volume for each additional test from same sample cup: 30 µL
  - ≤ 3 hours on board:

    Sample volume for first test: 150 µL

    Sample volume for each additional test from same sample cup: 30 µL
  - > 3 hours on board: Additional sample volume required. Refer to the ARCHITECT System Operations Manual, Section 5 for information on sample evaporation and volumes.
  - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare ARCHITECT Prolactin Calibrators and Controls.
  - Mix calibrator(s) and controls by gentle inversion before use.
  - Hold bottles **vertically** and dispense recommended volumes into each respective sample cup.
  - Recommended volumes:

    for each calibrator: 4 drops

    for each control: 3 drops
- Load samples.
  - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
- Press RUN.
- For additional information on principles of operation, refer to the ARCHITECT System Operations Manual, Section 3.
- For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.

Specimen Dilution Procedures

Specimens with a prolactin value exceeding 200 ng/mL are flagged with the code "> 200" and may be diluted using the Automated Dilution Protocol.

Automated Dilution Protocol

The system performs a 1:10 dilution of the specimen and automatically calculates the concentration of the specimen before dilution and reports the result.

If a sample run using the Automated Dilution Protocol is flagged with the code "< 6.0", it needs to be retested at a lower dilution or undiluted. The result and interpretation should not be reported.

For samples run with the 1:10 Automated Dilution Protocol which are flagged with the code "> 2000", manual dilutions should be performed as follows:

Manual Dilution Procedure

Suggested dilution: 1:40

1. Add 25 µL of the patient specimen to 975 µL of ARCHITECT Multi-Assay Manual Diluent (7D82-50).
2. The operator must enter the dilution factor in the Patient or Control order screen. The system will use this dilution factor to automatically calculate the concentration of the sample before dilution and report the result.

   If the operator does not enter the dilution factor, the reported result will be that of the diluted sample. This result (before dilution factor is applied) should be greater than 5 ng/mL. **The reported result must be multiplied by the dilution factor to obtain the concentration of the undiluted sample.**

For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

Calibration

- Test Calibrators 1 and 2 in duplicate. The calibrators should be priority loaded.

  A single sample of each control level must be tested to evaluate the assay calibration. Ensure that assay control values are within the ranges specified in the respective control package insert.
- Calibration Range: 0 - 200 ng/mL.
- Once an ARCHITECT Prolactin calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:
  - A reagent kit with a new lot number is used or
  - Controls are out of range.
- For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

Quality Control Procedures

The recommended control requirement for the ARCHITECT Prolactin assay is that a single replicate of each control level be tested once every 24 hours each day of use. If the quality control procedures in your laboratory require more frequent use of controls to verify test results, follow your laboratory-specific procedures.

Ensure that assay control values are within the concentration ranges specified in the control package insert.

Verification of Assay Claims

For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B.

The ARCHITECT Prolactin assay belongs to method group 1.

RESULTS

The ARCHITECT Prolactin assay utilizes a 4 Parameter Logistic Curve fit data reduction method (4PLC, X-weighted) to generate a calibration curve.

For information on alternate result units, refer to the **INSTRUMENT PROCEDURE, Alternate Result Units** section of this package insert.

Flags

Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the ARCHITECT System Operations Manual, Section 5.

LIMITATIONS OF THE PROCEDURE

- For diagnostic purposes, results should be used in conjunction with other data; e.g., symptoms, results of other tests, clinical impressions, etc.
- If the prolactin results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits such as ARCHITECT Prolactin that employ mouse monoclonal antibodies. Additional information may be required for diagnosis.[16, 17]
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. Patients routinely exposed to animals or to animal serum products can be prone to this interference, and anomalous values may be observed. Additional information may be required for diagnosis.[18]
- Prolactin may exist in alternate structural forms (e.g., macroprolactin)[19-22] which may exhibit variable levels of physiological activity.[23] In patients with elevated prolactin results, additional information may be required for diagnosis.

EXPECTED VALUES

The expected ranges for this assay were established by testing serum specimens from 100 apparently healthy males and 100 apparently healthy, nonpregnant females. The expected range for males includes the entire range of values. For the female expected range, the central 90 percent interval of all values is reported in the following table.

		Prolactin Values (ng/mL)	
Population	n	Median	Range
Males	100	6.99	3.46 - 19.40
Females	100	10.29	5.18 - 26.53

It is recommended that each laboratory establish its own expected ranges, which may be unique to the population it serves, depending on its demographics.

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

Precision was determined as described in Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) Protocol EP5-T2.[24] A three member buffered protein based panel was assayed, using a single lot of reagents, in replicates of two at two separate times per day for 20 days on two instruments. Data from this study are summarized in the following table.

				Mean	Within Run		Total	
Panel Member	Reagent Lot	Instrument	n	Conc Value (ng/mL)	SD	%CV	SD	%CV
1	1	1	80	6.93	0.266	3.8	0.323	4.7
1	1	2	80	7.05	0.223	3.2	0.310	4.4
2	1	1	80	18.24	0.537	2.9	0.748	4.1
2	1	2	80	17.92	0.477	2.7	0.655	3.7
3	1	1	80	35.86	1.098	3.1	1.302	3.6
3	1	2	80	35.25	0.793	2.3	1.165	3.3

Recovery

Known concentrations of prolactin were added to five aliquots of human serum. The concentration of prolactin was determined using the ARCHITECT Prolactin assay and the resulting percent recovery was calculated. The percent recovery of the ARCHITECT Prolactin assay ranged from 92.4% to 101.1% with an average of 95.8%.

Analytical Sensitivity

The analytical sensitivity of the ARCHITECT Prolactin assay was calculated to be better than 0.6 ng/mL (n = 24 runs). Analytical sensitivity is defined as the concentration at two standard deviations from the mean RLU value of the ARCHITECT Prolactin MasterCheck Level 0 (0.0 ng/mL), and represents the lowest measurable concentration of prolactin that can be distinguished from zero.

Specificity

Human serum specimens containing 13-16 ng/mL of prolactin were supplemented with follicle stimulating hormone (FSH), human chorionic gonadotropin (hCG), human growth hormone (hGH), human placental lactogen (hPL), luteinizing hormone (LH), or thyroid stimulating hormone (TSH) at specific levels. The results are stated in the following table.

Potential Cross Reactant	Concentration Tested	Cross Reactivity (%)
FSH	1,000 mIU/mL	0
hCG	100,000 mIU/mL	0
hGH	1,000 ng/mL	0.03
hPL	100,000 ng/mL	0
LH	5,000 mIU/mL	0.001
TSH	20,000 µIU/mL	0

Interference

Potential interference from hemoglobin, bilirubin, triglycerides, and protein was studied in the ARCHITECT Prolactin assay. The ARCHITECT Prolactin assay demonstrated the following interferences.

- Hemoglobin < 10% at 500 mg/dL
- Bilirubin < 10% at 20 mg/dL
- Triglycerides < 10% at 3000 mg/dL
- Protein < 10% at 2.0 g/dL and 12.0 g/dL

Accuracy by Correlation

The ARCHITECT Prolactin assay was compared to a commercially available diagnostic kit. The results of the specimen testing are shown in the following table.

Abbott ARCHITECT Prolactin vs. Abbott AxSYM Prolactin

Method	Number of Specimens	Intercept	Slope	Correlation Coefficient
Least Squares Linear Regression	597	0.55	0.98	0.995
Passing-Bablok Linear Regression*	597	0.49	0.99	0.995

In this evaluation, serum specimens tested ranged from 0.65 ng/mL to 185.74 ng/mL with the ARCHITECT Prolactin assay.

* A linear regression method with no special assumptions regarding the distribution of the samples and the measurement errors.[25]

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Key to Symbols

	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
CONJUGATE	Conjugate
CONTROL NO.	Control Number
DISTRIBUTED IN THE USA BY	Distributed in the USA by
INFORMATION FOR USA ONLY	Information needed for United States of America only
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
MICROPARTICLES	Microparticles
MULTI-ASSAY MANUAL DILUENT	Multi-Assay Manual Diluent
PRODUCT OF IRELAND	Product of Ireland
PRE-TRIGGER SOLUTION	Pre-Trigger Solution
REACTION VESSELS	Reaction Vessels
REAGENT LOT	Reagent Lot
REF	List Number
REPLACEMENT CAPS	Replacement Caps
SAMPLE CUPS	Sample Cups
SEPTUM	Septum
SN	Serial number
TRIGGER SOLUTION	Trigger Solution
WARNING: SENSITIZER	Warning: May cause an allergic reaction.
WASH BUFFER	Wash Buffer

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