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

See REAGENTS section for a full explanation of symbols used in reagent component naming.

Key to symbols used

- **REF**: List Number
- **LOT**: Lot Number
- **IVD**: In Vitro Diagnostic Medical Device
- **MASTER CAL**: Master Calibrator (1, 2)
- **CONTROL L**: Control Low, Medium, High (L, M, H)
- **CAL A**: Calibrator (A-F)
- **REAGENT PACK**: Reagent Pack
- **REACTION VESSELS**: Reaction Vessels
- **MATRIX CELLS**: Matrix Cells
- **SAMPLE CUPS**: Sample Cups
- **CONSULT INSTRUCTIONS FOR USE**: Consult instructions for use
- **MASTER CALIBRATION BARCODE**: Master Calibration Barcode
- **CHECKSUM**: Checksum

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International: Call your Abbott Representative

See REAGENTS section for a full explanation of symbols used in reagent component naming.
LH, hCG, and TSH. The β subunit of FSH is unique and confers its manner, with rapid fluctuations over the normal range. The use of oral contraceptives usually results in reduction of gonadotropin levels due to negative feedback by these steroids.5 Determination of serum FSH, following administration of GnRH may release of GnRH or from a lack of response of the pituitary to GnRH. Because of the negative feedback mechanisms regulating gonadotropin release, FSH and LH from the pituitary is under negative feedback control by the gonadal tissues.2 FSH promotes follicular development in the ovary and gametogenesis in the testis.3,4 The gonadotroph cells of the anterior pituitary secrete both FSH and LH in response to gonadotropin releasing hormone (LHRH or GnRH) from the medial basal hypothalamus.1 Both FSH and LH are secreted in a pulsatile manner, with rapid fluctuations over the normal range.5,7 The pulsatility of FSH is less pronounced than that of LH. Release of both FSH and LH from the pituitary is under negative feedback control by the gonadal tissues.2 FSH in mature females acts to stimulate development of the ovarian follicle. Circulating FSH levels vary throughout the menstrual cycle in response to estradiol and progesterone. A small, but significant increase in circulating FSH accompanies the mid-cycle LH surge. However, the physiological significance of this increase is unknown. Circulating levels of FSH decline in the luteal phase in response to estradiol and progesterone production by the developing corpus luteum.7 At menopause ovarian function is diminished, with concomitant decrease in estradiol secretion. FSH and LH then increase significantly in response to diminished feedback inhibition of gonadotropin release.4,7 In males, FSH, LH, and testosterone regulate spermatogenesis by the Sertoli cells in the seminiferous tubules of the testes. FSH is less sensitive to feedback inhibition by testosterone than is LH and is thought to be regulated independently by the hypothalamic-pituitary axis.5 Because of the negative feedback mechanisms regulating gonadotropin release, elevated concentrations of LH and FSH are indicative of gonadal failure when accompanied by low concentrations of the gonadal steroids. In males, these observations suggest primary testicular failure or anorchia.6 FSH may also be elevated in Klinefelter’s syndrome (seminiferous tubule dysgenesis) or as a consequence of Sertoli cell failure.7 In females, situations in which FSH is elevated and gonadal steroids are depressed include menopause, premature ovarian failure, and ovariectomy, while with polycystic ovarian syndrome the LH/FSH ratio may be increased.8 Abnormal FSH concentrations may also indicate dysfunction of the hypothalamic-pituitary axis. In sexually mature adults, FSH deficiency, together with low concentrations of LH and sex steroids, may indicate hypogonadism.8 This can result either from a decrease in the release of GnRH or from a lack of response of the pituitary to GnRH. Determination of serum FSH, following administration of GnRH may allow differentiation of these two conditions.5,7 The use of oral contraceptives usually results in reduction of gonadotropin levels due to negative feedback by these steroids.2
FSH Calibrators (9C06-02)

6 Bottles (4 mL each) of FSH Calibrators. Calibrator A contains processed bovine serum, and Calibrators B-F contain FSH (human) prepared in processed bovine serum to yield the following concentrations:

<table>
<thead>
<tr>
<th>Concentration (mIU/mL)</th>
<th>Bottle</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>CONTROL A</td>
</tr>
<tr>
<td>1</td>
<td>CONTROL B</td>
</tr>
<tr>
<td>10</td>
<td>CONTROL C</td>
</tr>
<tr>
<td>50</td>
<td>CONTROL D</td>
</tr>
<tr>
<td>100</td>
<td>CONTROL E</td>
</tr>
<tr>
<td>150</td>
<td>CONTROL F</td>
</tr>
</tbody>
</table>

Preservatives: Sodium Azide.

The calibrators are manufactured by addition of Follicle Stimulating Hormone (FSH) of known concentration to obtain a target concentration. The concentration is referenced against World Health Organization (WHO) FSH 1\(^{st}\) International Standard (92/510).

CONTROLS

FSH Controls (9C06-12)

3 Bottles (4 mL each) of FISH Controls contain FSH (human) prepared in calf serum to yield the following concentration ranges:

<table>
<thead>
<tr>
<th>Concentration (mIU/mL)</th>
<th>Bottle</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>CONTROL A</td>
</tr>
<tr>
<td>3.5</td>
<td>CONTROL B</td>
</tr>
<tr>
<td>6.5</td>
<td>CONTROL C</td>
</tr>
<tr>
<td>25</td>
<td>CONTROL M</td>
</tr>
<tr>
<td>18</td>
<td>CONTROL N</td>
</tr>
<tr>
<td>32</td>
<td>CONTROL Q</td>
</tr>
<tr>
<td>75</td>
<td>CONTROL U</td>
</tr>
<tr>
<td>53</td>
<td>CONTROL X</td>
</tr>
<tr>
<td>97</td>
<td>CONTROL Z</td>
</tr>
</tbody>
</table>

Preservatives: Sodium Azide.

OTHER REAGENTS

AxSYM Probe Cleaning Solution (9A35-05)

Solution 3 (Matrix Cell Wash) (8A81-04)

Preservative: Sodium Azide.

Solution 4 (Line Diluent) (8A46)

TRIS Buffer. Preservatives: Sodium Azide and Antimicrobial Agents.

Solution 3 (Matrix Cell Wash) containing 0.3 M Sodium Chloride in processed bovine serum, and Calibrators B-F contain FSH

Preservative: Sodium Azide.

AxSYM FSH Assay Parameters

Assay Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assay Name</td>
<td>FSH</td>
</tr>
<tr>
<td>Assay Type</td>
<td>MEIA</td>
</tr>
<tr>
<td>Assay File</td>
<td>Revision 1</td>
</tr>
<tr>
<td>Assay Number</td>
<td>37</td>
</tr>
<tr>
<td>Assay Version</td>
<td>*</td>
</tr>
<tr>
<td>Assay File Revision</td>
<td>*</td>
</tr>
<tr>
<td>Assay Enabled</td>
<td>ON</td>
</tr>
<tr>
<td>Assay Type</td>
<td>MIA</td>
</tr>
<tr>
<td>Standard Cal Reps</td>
<td>2</td>
</tr>
<tr>
<td>Master Cal Reps</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>Cal A Concentration</td>
<td>0.00</td>
</tr>
<tr>
<td>Cal B Concentration</td>
<td>1.00</td>
</tr>
<tr>
<td>Cal C Concentration</td>
<td>10.00</td>
</tr>
<tr>
<td>Cal D Concentration</td>
<td>50.00</td>
</tr>
<tr>
<td>Cal E Concentration</td>
<td>100.00</td>
</tr>
<tr>
<td>Cal F Concentration</td>
<td>150.00</td>
</tr>
<tr>
<td>Master Calibrator 1 Concentration</td>
<td>0.00</td>
</tr>
<tr>
<td>Master Calibrator 2 Concentration</td>
<td>100.00</td>
</tr>
<tr>
<td>Default Dilution Protocol</td>
<td>UNDILUTED</td>
</tr>
<tr>
<td>Default Calibration Method</td>
<td>Standard Cal</td>
</tr>
</tbody>
</table>

HANDLING PRECAUTIONS

- Do not use Solution 1 (MUP) beyond the expiration date or a maximum of 14 days on-board the AxSYM System. When loading new Solution 1 (MUP), it is important to immediately tighten the instrument cap for MUP to minimize exposure to air. Prolonged exposure of MUP to air may compromise performance.
- Do not mix reagents from different reagent packs.
- Refer to the AxSYM System Operations Manual, Sections 7 and 8, for a more detailed discussion of the safety and handling precautions during system operation.

STORAGE INSTRUCTIONS

The AxSYM FSH Reagent Pack must be stored at 2-8°C (do not freeze). The FSH Calibrators and FSH Controls must be stored at 2-8°C. The AxSYM FSH Reagent Pack, Calibrators and Controls may be used immediately after removing them from the refrigerator. Calibrators and Controls should be returned to 2-8°C storage immediately after use. Reagents are stable until the expiration date when stored and handled as directed.

The AxSYM FSH Reagent Pack may be on-board the AxSYM System for a maximum of 336 cumulative hours; for example, 42 eight hour shifts. Recalibration may be required to obtain maximum on-board reagent stability. More frequent use of controls may be required to monitor reagent performance within the same lot. Refer to the AxSYM System Operations Manual, Appendices, for further information on tracking on-board time.

Solution 1 (MUP) must be stored at 2-8°C (do not freeze). It may be used immediately after removing it from the refrigerator. MUP may be on-board the AxSYM System for a maximum of 14 days. After 14 days, it must be discarded.

The AxSYM Probe Cleaning Solution, Solution 3 (Matrix Cell Wash) and Solution 4 (Line Diluent) must be stored at 15-30°C.

INSTRUMENT PROCEDURE

Assay File Installation

The AxSYM FSH Assay File must be installed on the AxSYM System from one of the following software disks prior to performing FSH assays:

- BAB9-01, or higher (112 hours on-board Stability)
- JDOL-01, or higher (336 hours on-board Stability)

Refer to the AxSYM System Operations Manual, Section 2, for proper installation procedures.

AxSYM FSH Assay Parameters

The default values for the assay parameters used for the AxSYM FSH assay are listed below. These parameters can be displayed and edited according to the procedure in the AxSYM System Operations Manual, Section 2. In order to obtain values for the parameters with an asterisk (*), review the specific assay Parameter screen. Press PRINT to print the assay parameters. Assay parameters that can be edited contain a (*) symbol.
Materials Required but Not Provided

- **AxSYM System**
- **9C06-12** FSH Controls
- **9C06-02** FSH Calibrators or
- **7400-32** AxSYM FSH Master Calibrators
- **8A47-04**
- **8A81-04**
- **8A46**
- **9A35-05** AxSYM FSH CLEANING SOLUTIONS
- **8A76-01** Pipettes/pipette tips (optional) to deliver the volumes specified on the Order screen.

**CAUTION:**
- When manually dispensing sample into sample cups, verify that the dispensing equipment does not introduce cross-contamination and deliver the specified sample volume.
- For optimal performance, it is important to follow the routine maintenance procedures defined in the AxSYM System Operations Manual, Section 9. If your laboratory requires more frequent maintenance, follow those procedures.

**AxSYM FSH PROCEDURE**

**Assay Procedure**

Sections 5 and 6 of the AxSYM System Operations Manual can be easily removed for use at the instrument. They contain detailed steps for performing assay calibration and sample testing procedures.

**Materials Required but Not Provided**

- **AxSYM System**
- **9C06-12** FSH Controls
- **9C06-02** FSH Calibrators or
- **7400-32** AxSYM FSH Master Calibrators
- **8A47-04**
- **8A81-04**
- **8A46**
- **9A35-05** AxSYM FSH CLEANING SOLUTIONS
- **8A76-01** Pipettes/pipette tips (optional) to deliver the volumes specified on the Order screen.

**CAUTION:**
- When operating the AxSYM System, always observe the following:
  - The System status must be WARMING, PAUSED, READY or STOPPED before adding or removing sample segments, reagent packs or reaction vessels (RV's).
  - Do not open the Interior Waste Door or the AxSYM Processing Center Cover while any test is in process. If opened, all processing will stop. Tests in process will be terminated and must be repeated.
  - When testing is completed, it is recommended that samples and the AxSYM FSH Reagent Pack are removed from the Sampling Center to maximize the on-board reagent pack use. Store at 2-8°C.

**SPECIMEN DILUTION PROCEDURES**

**Automated Dilution Protocol**

FSH specimens **CANNOT** be diluted automatically on the System.

**Manual Dilution Protocol**

Patient specimens with FSH concentrations reported as greater than 150 mIU/mL may be diluted using a manual dilution of the specimen with FSH Calibrator A (0 mIU/mL) or AxSYM FSH Master Calibrator 1 (0 mIU/mL). A 1:2 dilution is adequate for most specimens. The dilution should be performed so that the diluted test results read greater than the sensitivity of the assay (0.37 mIU/mL). Perform the test using this manually diluted specimen. The concentration reported by the AxSYM System must be multiplied by the manual dilution factor to obtain the final specimen concentration.
QUALITY CONTROL PROCEDURES

CALIBRATION

The AxSYM FSH Assay must be calibrated using either a Master Calibration (2-point), or a Standard Calibration (6-point) procedure. The use of a particular calibration procedure is dependent on individual laboratory policy.

Master Calibration

Each AxSYM FSH Reagent Pack is shipped with a bar coded label insert that contains the Master Curve information for that specific lot of reagents. When using a lot number for the first time, the bar coded Master Curve information must be entered into the AxSYM System. Refer to the AxSYM System Operations Manual, Section 6, for additional information on entering Master Curve bar codes. Once this bar code information is entered, a Master Calibration must be performed.

To perform an AxSYM FSH Master Calibration, test Master Calibrators 1 and 2 in duplicate. A single sample of all levels of FSH controls must be tested as a means of evaluating the assay calibration.

Standard Calibration

The Standard Calibration procedure may be used without prior entry of the bar coded Master Curve information. To perform an AxSYM FSH Standard Calibration, test Calibrators A, B, C, D, E, and F in duplicate. A single sample of all levels of FSH controls must be tested as a means of evaluating the assay calibration.

Once the AxSYM FSH calibration is accepted and stored, all subsequent samples may be tested without further calibration unless a reagent pack with a new lot number is used. Refer to the AxSYM System Operations Manual, Section 6, for:
- Setting up an assay calibration
- When recalibration may be necessary
- Calibration verification

The AxSYM System verifies that the results of an assay calibration meet the specifications assigned to selected validity parameters. An error message occurs when the calibration fails to meet a specification. Refer to the AxSYM System Operations Manual, Section 10, for an explanation of the corrective actions for the error code. For a description of the flags that may appear in this field, refer to the AxSYM System Operations Manual, Section 2.

Flag:

Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the AxSYM System Operations Manual, Section 2.

LIMITATION OF THE PROCEDURE

- For diagnostic purposes, the AxSYM FSH results should be used in conjunction with other data; e.g., symptoms, results of other tests, clinical impressions, etc.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMAs). Such specimens may show either falsely elevated or depressed values when tested with assay kits which employ mouse monoclonal antibodies.16,17 These specimens should not be assayed with the AxSYM FSH assay.
- Refer to the SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS section in this package insert.

EXPECTED VALUES

The suggested normal range for the AxSYM FSH assay represents the FSH values obtained from 150 normal males, 35 post-menopausal females (not on hormone replacement therapy) and 44 normal cycling females. For this study, the follicular phase was defined as the period of time from 10 to 4 days prior to the mid-cycle peak. The luteal phase was defined as the period of time from 4 to 10 days following the mid-cycle peak. Cycle days were synchronized to the mid-cycle peak (the day when LH values are most elevated). The results are presented in the following table. (Note: 44 women participated in the study for serial blood draws. At the time of testing for AxSYM FSH, only 42 of the midcycle samples were available for testing. Samples from all 44 women were included in the follicular and luteal phase expected values testing.)

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>n</th>
<th>Mean</th>
<th>Range (central 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>150</td>
<td>3.77</td>
<td>1.15 – 12.51</td>
</tr>
<tr>
<td>Normally Menstruating Females</td>
<td>144</td>
<td>4.94</td>
<td>3.09 – 7.90</td>
</tr>
<tr>
<td>Post-Menopausal Females</td>
<td>35</td>
<td>61.15</td>
<td>30.07 – 106.32</td>
</tr>
</tbody>
</table>

* Median value is displayed

It is recommended that each laboratory establish its own reference range that is appropriate for the laboratory’s patient population (i.e., a normal range that reflects the type of specimen and demographic variables such as age and sex, as applicable).

An error message occurs when the calibration fails to meet a specification. Refer to the AxSYM System Operations Manual, Section 10, when this error message is obtained.

The AxSYM FSH utilizes a four parameter logistic curve fit (4PLC) data reduction method to generate a calibration curve.
SPECIFIC PERFORMANCE CHARACTERISTICS

**PRECISION**

Precision was determined as described in National Committee for Clinical Laboratory Standards (NCCLS) protocol EP3-T2. A three member call serum based panel was assayed, using a single lot of reagents, in replicates of 2 at two separate times per day for twenty days. Data from this study are summarized below.

### PANEL MEMBER 1

<table>
<thead>
<tr>
<th>Cross Reactant</th>
<th>Tested</th>
<th>Within Run</th>
<th>Between Run</th>
<th>Between Day</th>
<th>Total Run</th>
<th>SD</th>
<th>CV(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCG</td>
<td>4</td>
<td>79.86</td>
<td>80.00</td>
<td>5.47</td>
<td>5.94</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>TSH</td>
<td>4</td>
<td>26.76</td>
<td>26.30</td>
<td>26.35</td>
<td>26.76</td>
<td>0.20</td>
<td>3.72</td>
</tr>
</tbody>
</table>

**SPECIFICITY**

The AxSYM FSH assay demonstrated the stated interference in the presence of the following:

- **Bilirubin**: <5% interference at 20 mg/dL
- **Nhemoglobin**: <5% interference at 1000 mg/dL
- **Triglycerides**: <10% interference at 1000 mg/dL

**INTERFERENCE**

The AxSYM FSH assay demonstrated the stated interference in the presence of the following:

- **Bilirubin**: <5% interference at 20 mg/dL
- **Nhemoglobin**: <5% interference at 1000 mg/dL
- **Triglycerides**: <10% interference at 1000 mg/dL

**CORRELATION**

The Abbott AxSYM FSH assay was compared to the ARCHITECT FSH assay. The result of the specimen testing is shown in the following table.

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Intercept</th>
<th>Slope</th>
<th>Correlation Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Least Squares Linear Regression</td>
<td>627.0</td>
<td>0.25</td>
<td>0.99</td>
</tr>
<tr>
<td>Passing-Bablok</td>
<td>627.0</td>
<td>0.12</td>
<td>0.97</td>
</tr>
</tbody>
</table>

**ACCURACY BY RECOVERY**

Accuracy by Recovery of this assay was designed to be ± 15% of the concentration range (WHO) 1st International Standard (IS) FSH 92/510 were added to 11 aliquots of human serum at 2 concentration levels (20 mIU/mL and 40 mIU/mL). The concentration of FSH was determined using the AxSYM FSH assay. The mean recovery of WHO 1st IS FSH is 110.48%.

**SENSITIVITY**

The upper 95% limit of the sensitivity determination for AxSYM FSH Assay was 0.37 mIU/mL (n = 72 runs in replicates of 10). Sensitivity is defined as the concentration at 2 standard deviations from the mean of the distribution of the samples and the measurement errors.19

**SPECIFICITY**

Sensitivity by Recovery of this assay was designed to be ± 15% of the concentration range.

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**BIBLIOGRAPHY**


AxSYM and ARCHITECT are trademarks of Abbott Laboratories, Abbott Park, IL, USA.

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