# 3rd Generation TSH

This package insert must be read carefully prior to use. 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.

## Key to symbols used

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>REF</strong></td>
<td>List Number</td>
</tr>
<tr>
<td><strong>IVD</strong></td>
<td>In Vitro Diagnostic Medical Device</td>
</tr>
<tr>
<td><strong>LOT</strong></td>
<td>Lot Number</td>
</tr>
<tr>
<td><strong>STANDARD CAL</strong></td>
<td>Standard Calibrator (A-F)</td>
</tr>
<tr>
<td><strong>CONTROL</strong></td>
<td>Control Low, Medium, High (L, M, H)</td>
</tr>
<tr>
<td><strong>REAGENT PACK</strong></td>
<td>Reagent Pack</td>
</tr>
<tr>
<td><strong>i</strong></td>
<td>Manufacturer</td>
</tr>
</tbody>
</table>

See **REAGENTS** section for a full explanation of symbols used in reagent component naming.
elevated basal TSH levels are often seen despite significant reduction in T4 and/or hypothalamic or pituitary disease, 
metabolically active thyroid hormones, thyroxine (T4) and triiodothyronine (T3), by interacting with a specific receptor on the thyroid cell surface. T3 and T4 are responsible for regulating diverse biochemical processes throughout the body which are essential for normal development and metabolic and neural activity.

The synthesis and secretion of TSH is stimulated by thyrotropin releasing hormone (TRH), the hypothalamic tripeptide, in response to low levels of circulating thyroid hormones. Elevated levels of T3 and T4 suppress the production of TSH via a classic negative feedback mechanism. Recent evidence also indicates that somatostatin and dopamine exert inhibitory control over TSH release, suggesting that the hypothalamus may provide both inhibitory and stimulatory influence on pituitary TSH production. Failure at any level of regulation of the hypothalamic-pituitary-thyroid axis will result in either underproduction (hypothyroidism) or overproduction (hyperthyroidism) of T3 and/or T4.

In cases of primary hypothyroidism, T3 and T4 levels are low and TSH levels are significantly elevated. In the case of pituitary dysfunction, due to either intrinsic hypothalamic or pituitary disease, i.e., central hypothyroidism, normal or marginally elevated basal TSH levels are often seen despite significant reduction in T4 and/or T3 levels. These inappropriately high TSH values are due to a reduction in TSH bioactivity which is frequently observed in such cases. Routine TRH stimulation is advised to confirm the diagnosis in such cases. Secondary hypothyroidism typically results in an impaired TSH response to TRH, while in tertiary hypothyroidism the TSH response to TRH may be normal, prolonged, or exaggerated.

Primary hyperthyroidism (e.g., Grave’s Disease, or nodular goiter) is associated with high levels of thyroid hormones and depressed or undetectable levels of TSH. The TRH stimulation test has been used in diagnosis of hyperthyroidism. Hyperthyroid patients show a subnormal response to the TRH test. Failure at any level of regulation of the hypothalamic-pituitary-thyroid axis will result in either underproduction (hypothyroidism) or overproduction (hyperthyroidism) of T3 and/or T4.

Earlier assays for serum TSH lacked the sensitivity to be used as a primary test of thyroid function. Functional sensitivity has replaced analytical sensitivity as a means of assessing low concentration accuracy. The American Thyroid Association has formally recommended the use of functional sensitivity as the means to quantify the sensitivity of TSH assays, although analytical sensitivity is still widely used. Third generation TSH assays, which discriminate between hyperthyroid and euthyroid patients, exhibit less than 20% CV at < 0.02 μIU/mL. The functional sensitivity of the AxSYM 3rd Generation TSH assay meets these criteria (see SPECIFIC PERFORMANCE CHARACTERISTICS section in this assay package insert). Other thyroid tests (Free T4, Total T4, T3-Uptake, Total T3, and Free T3) combined with the ability to accurately measure low levels of TSH, improve the efficiency of thyroid diagnosis.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE
The AxSYM 3rd Generation TSH assay is based on Microparticle Enzyme Immunoassay (MEIA) technology. The AxSYM 3rd Generation TSH Reagents and sample are pipetted in the following sequence:

SAMPLING CENTER
• Sample and all AxSYM 3rd Generation TSH Reagents required for one test are pipetted into the Sampling Probe into various wells of a Reaction Vessel (RV).
• Sample and anti-hTSH (human Thyroid Stimulating Hormone) coated microparticles are combined in a well of the RV forming an antibody-antigen complex.
• Biotinylated anti-hTSH Conjugate (conjugate 1) is pipetted into a second well of the RV.
• Wash Buffer is pipetted into a third well of the RV.
• Anti-Biotin:Alkaline Phosphatase Conjugate (conjugate 2) is pipetted into a fourth well of the RV.

The RV is immediately transferred into the Processing Center. Further pipetting is done in the Processing Center by the Processing Probe.

PROCESSING CENTER
• An aliquot of the sample/microparticle mixture, containing the antibody-antigen complex bound to the microparticles, is transferred to the Matrix Cell. The microparticles bind irreversibly to the glass fiber matrix while unbound material is removed by a buffer wash.
• Conjugate 1 is then dispensed onto the Matrix Cell and allowed to bind to the TSH of the antibody-antigen complex, forming an antibody-antigen-antibody complex.
• The Matrix Cell is washed to remove unbound conjugate.
• Conjugate 2 is then dispensed onto the Matrix Cell and binds to conjugate 1, to form the biotin anti-biotin (BAB) complex.
• The Matrix Cell is washed to remove unbound conjugate.
• The substrate, 4-Methylumbelliferyl Phosphate, is added to the Matrix Cell and the fluorescent product formed is measured by the MEIA optical assembly.

For further information, refer to the AxSYM System Operations Manual, Section 3.

REAGENTS
REAGENT PACK, 100 TESTS
AxSYM 3rd Generation TSH Reagent Pack (7K49-22)
• 1 Bottle (8.6 mL) Anti-hTSH (Mouse, Monoclonal) coated Microparticles in TRIS buffer with protein (bovine) stabilizer. Preservative: Sodium Azide. (Reagent Bottle 1)
• 1 Bottle (12.8 mL) Biotinylated anti-hTSH (Goat) Conjugate in TRIS buffer with protein (fish) stabilizer. Preservative: Sodium Azide. (Reagent Bottle 2)
• 1 Bottle (13.7 mL) Anti-Biotin (Rabbit):Alkaline Phosphatase Conjugate in TRIS buffer with protein (fish) stabilizer. Preservative: Sodium Azide. (Reagent Bottle 3)
• 1 Bottle (47.0 mL) Wash Buffer containing surfactant. (Reagent Bottle 4)

a 7K49-22 includes an AxSYM 3rd Generation TSH Reagent Pack (100 tests), Reaction Vessels (100 each), and Matrix Cells (100 each).

CALIBRATORS
AxSYM 3rd Generation TSH Standard Calibrators (7K49-02)
6 Bottles (4 mL each) of AxSYM 3rd Generation TSH Standard Calibrators. Calibrator A contains TRIS buffer with protein (bovine) stabilizer. Calibrators B through F contain TSH (recombinant) in TRIS buffer with protein (bovine) stabilizer to yield the following concentrations: 0.0, 0.5, 6.0, 12.0, 25.0, 40.0 μIU/mL.

Preservative: Sodium Azide.

b The calibrators are manufactured gravimetrically and are referenced to the World Health Organization (W.H.O.) Third International Standard 81/565 for TSH (Thyroid Stimulating Hormone) at each concentration level.

CONTROLS
AxSYM 3rd Generation TSH Controls (7K49-11)
3 Bottles (8 mL each) of AxSYM 3rd Generation TSH Controls contain TSH (recombinant) in TRIS buffer with protein (bovine) stabilizer to yield the following concentration ranges:

Preservative: Sodium Azide.

The AxSYM 3rd Generation TSH default result unit is μIU/mL. An alternate result unit (mIU/L) may be selected for reporting results (Assay Parameter 45). The conversion factor used by the AxSYM System is 1.0.
OTHER REAGENTS
AxSYM Probe Cleaning Solution (9A35-05)

PROBE CLEANING SOLUTION 2 Bottles (220 mL each) AxSYM Probe Cleaning Solution containing 2% Tetraethylammonium Hydroxide (TEAH). Solution 1 (MUP) (8A47-04)

SOLUTION 1 [MUP] 4 Bottles (230 mL each) Solution 1 (MUP) containing 4-Methylumbelliferyl Phosphate, 1.2 mM, in AMP buffer. Preservative: Sodium Azide. Solution 3 (Matrix Cell Wash) (8A1-04)

SOLUTION 3 [MATRIX CELL WASH] 4 Bottles (1000 mL each) Solution 3 (Matrix Cell Wash) containing 0.3 M Sodium Chloride in TRIS buffer. Preservatives: Sodium Azide and Antimicrobial Agents. Solution 4 (Line Diluent) (8A46)

SOLUTION 4 [LINE DILUENT] 1 Bottle (10 L) Solution 4 (Line Diluent) containing 0.1 M Phosphate buffer. Preservatives: Sodium Azide and Antimicrobial Agent.

WARNINGS AND PRECAUTIONS
For In Vitro Diagnostic Use Only.

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 with appropriate biosafety practices.

- This product contains sodium azide; for a specific listing, refer to the REAGENTS section. Contact with azides liberates very toxic gas. This material and its container must be disposed of in a safe way.

For product not classified as dangerous per European Directive 1999/45/EC as amended - Safety data sheet available for professional user on request.

HANDLING PRECAUTIONS

- The components (Reagents, Calibrators, and Controls) of the AxSYM 3rd Generation TSH assay are not interchangeable with the components of other Abbott TSH assays.

- AxSYM 3rd Generation TSH Reagents are susceptible to bubbles/foaming and require inspection and removal of bubbles before loading. Refer to the AxSYM System Operations Manual, Section 9.

- 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 use reagent pack beyond the expiration date or a maximum of 336 cumulative hours on-board the AxSYM System.

- 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

AxSYM 3rd Generation TSH Reagent Pack must be stored at 2-8°C (do not freeze). The AxSYM 3rd Generation TSH Standard Calibrators and Controls must be stored at 2-8°C. The AxSYM 3rd Generation TSH Reagent Pack, Standard Calibrators, and Controls may be used immediately after removing them from the refrigerator. Return standard calibrators and controls to 2-8°C storage immediately after each use.

AxSYM 3rd Generation TSH Reagents are stable until the expiration date when stored and handled as directed. The AxSYM 3rd Generation TSH 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. After 336 hours, the reagent pack must be discarded. Refer to the AxSYM System Operations Manual, Sections 2, 5, and Appendix C, 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.

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 3rd Generation TSH Assay File must be installed on the AxSYM System from the Thyroid Assay Disk, 2G37-03 or higher, prior to performing AxSYM 3rd Generation TSH assays. Refer to the AxSYM System Operations Manual, Section 2, for proper installation procedures.

AxSYM 3rd Generation TSH ASSAY PARAMETERS

The default values for the assay parameters used for the AxSYM 3rd Generation TSH assay are listed in the Assay Parameters table. Assay parameters that can be edited contain a (>) symbol. 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 Parameters screen. Press PRINT to print the assay parameters.

ASSAY PARAMETERS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Long Assay Name (English): 3RD_GEN_TSH</td>
</tr>
<tr>
<td>6</td>
<td>Abbrev Assay Name (English): TSH_3GEN</td>
</tr>
<tr>
<td>11</td>
<td>Assay Number: 213</td>
</tr>
<tr>
<td>12</td>
<td>Assay Version: *</td>
</tr>
<tr>
<td>13</td>
<td>Calibration Version:</td>
</tr>
<tr>
<td>14</td>
<td>Assay File Revision: *</td>
</tr>
<tr>
<td>15</td>
<td>Assay Enabled &gt; ON</td>
</tr>
<tr>
<td>17</td>
<td>Assay Type: MEIA</td>
</tr>
<tr>
<td>18</td>
<td>Standard Cal Reps &gt; 2</td>
</tr>
<tr>
<td>21</td>
<td>Cal A Concentration: 0.000</td>
</tr>
<tr>
<td>22</td>
<td>Cal B Concentration: 0.500</td>
</tr>
<tr>
<td>23</td>
<td>Cal C Concentration: 6.000</td>
</tr>
<tr>
<td>24</td>
<td>Cal D Concentration: 12.000</td>
</tr>
<tr>
<td>25</td>
<td>Cal E Concentration: 25.000</td>
</tr>
<tr>
<td>26</td>
<td>Cal F Concentration: 40.000</td>
</tr>
<tr>
<td>43</td>
<td>Default Dilution Protocol &gt; UNDILUTED</td>
</tr>
<tr>
<td>44</td>
<td>Default Calibration Method &gt; Standard Cal</td>
</tr>
<tr>
<td>45</td>
<td>Selected Result Concentration Units &gt; μIU/mL</td>
</tr>
<tr>
<td>46</td>
<td>Selected Result Decimal Places &gt; 3</td>
</tr>
<tr>
<td>91</td>
<td>Low Range Undiluted: *</td>
</tr>
<tr>
<td>92</td>
<td>High Range Undiluted: *</td>
</tr>
</tbody>
</table>

NOTE: Parameter 45 can be edited to the alternate result unit, mIU/L.

NOTE: Parameter 46 cannot be edited.


SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

- Human serum (including serum collected in serum separator tubes [SST]) or plasma (collected in lithium heparin, sodium heparin, tripotassium EDTA, or potassium oxalate tubes) may be used in the AxSYM 3rd Generation TSH assay. Other anticoagulants have not been tested with the AxSYM 3rd Generation TSH assay. Follow the manufacturer’s processing instructions for serum or plasma collection tubes.

- The AxSYM System does not provide the capability to verify sample type. It is the responsibility of the operator to verify the correct sample type(s) is/are used in the AxSYM 3rd Generation TSH assay.

- Ensure that complete clot formation 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.

- For optimal results, specimens should be free of fibrin, red blood cells, lipids, or other particulate matter.

- Multiple freeze/thaw cycles should be avoided. Specimens must be mixed thoroughly after thawing, by LOW speed vortexing or by gently inverting, and centrifuged prior to use to remove particulate matter and to ensure consistency in the results.

- Specimens may be stored for up to 7 days at 2-8°C prior to being tested. Serum or plasma should be separated from the clot or red blood cells within 24 hours after collection. If testing will be delayed more than 7 days, specimens should be stored frozen (-20°C or colder). Patient specimens must be mixed and centrifuged after any freeze/thaw cycle or to remove red blood cells or other particulate matter. Specimens stored frozen at -20°C or colder for 6 months did not show performance differences.
To minimize the effects of evaporation, all samples (patient specimens, controls, and calibrators) should be tested within 3 hours of being placed on-board the AxSYM System. Refer to the AxSYM System Operations Manual, Section 5, for a more detailed discussion of on-board sample storage constraints.

Do not use heat-inactivated specimens.

Performance has not been established using cadaver specimens or body fluids other than human serum or plasma.

Specimens with obvious microbial contamination should not be used.

Inspect all samples for bubbles. Remove bubbles prior to analysis.

When shipped, specimens must be packaged and labeled in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances. Specimens must be shipped frozen on dry ice. Prior to freezing, serum or plasma specimens must be removed from the clot or red blood cells.

SAMPLE VOLUME

The sample volume required to perform a single undiluted 3rd generation TSH test on the AxSYM System varies depending on the type of sample container used. For sample cups, both ROUTINE and STAT tests require 224 μL. For every additional AxSYM 3rd Generation TSH test performed (ROUTINE or STAT) from the same sample container, an additional 174 μL of sample is required.

The sample cup minimum volumes for both STAT and ROUTINE tests are calculated by the AxSYM System. They are displayed on the Order screen at the time the test(s) is(are) ordered. The sample cup STAT minimum volume is printed in the Orderlist Report. When using Host Order Query, the Orderlist screen information and the Orderlist Report are not available. Refer to the AxSYM System Operations Manual, Section 5, for a description of the Host Order Query option.

If the assay is configured for auto retest or reflex testing, the sample volume needed for the additional test will not be displayed on the Order screen at the time the test(s) is(are) ordered. Therefore, the total sample volume for one auto retest should include an additional 174 μL of sample. Refer to the following table for additional sample volume requirements for reflex testing.

<table>
<thead>
<tr>
<th>AxSYM Assay</th>
<th>REF</th>
<th>Additional Sample Volume (μL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free T4</td>
<td>7A54 / 7K51</td>
<td>55</td>
</tr>
<tr>
<td>Total T4</td>
<td>7A56</td>
<td>39</td>
</tr>
<tr>
<td>T-Uptake</td>
<td>7A56</td>
<td>44</td>
</tr>
<tr>
<td>Total T3</td>
<td>7A56</td>
<td>88</td>
</tr>
<tr>
<td>Free T3</td>
<td>7A53 / 7K50</td>
<td>130</td>
</tr>
</tbody>
</table>

If the assay is configured for auto dilution, include an additional 65 μL of sample volume in the sample container when ordering tests. To obtain the recommended volume requirements for the AxSYM 3rd Generation TSH Standard Calibrators and Controls, hold the bottles vertically and dispense 9 drops of each calibrator or 5 drops of each control into each respective sample cup. Refer to the AxSYM System Operations Manual, Section 5, for sample volume requirements in primary or aliquot tubes and calibrator/control requirements for multiple reagent lots.

AxSYM 3rd Generation TSH PROCEDURE

Materials Provided

- 7K49-22 AxSYM 3rd Generation TSH Reagent Kit, containing:
  - AxSYM 3rd Generation TSH REAGENT PACK
  - 100 REACTION VESSELS
  - 100 MATRIX CELLS

Materials Required But Not Provided

- AxSYM System
- 7K49-11 AxSYM 3rd Generation TSH Controls
- 7K49-02 AxSYM 3rd Generation TSH Standard Calibrators
- 8A47-04 SOLUTION 1 MUP
- 8A81-04 SOLUTION 3 MATRIX CELL WASH
- 8A46 SOLUTION 4 LINE DILUENT
- 9A35-05 AxSYM PROBE CLEANING SOLUTION
- 8A76-01 SAMPLE CUPS
- Pipettes or pipette tips (optional) to deliver the volumes specified on the Order screen

CAUTION:

- When manually dispensing sample into sample cups, verify that dispensing equipment does not introduce cross contamination and delivers the specified sample volume. Use a separate pipette tip for each sample. Use accurately calibrated equipment.

- 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.

Assay Procedure

Sections 5 and 6 of the AxSYM System Operations Manual contain detailed steps for performing assay calibration and sample testing procedures. Prior to ordering tests, confirm that the System inventory of Matrix Cells, bulk solutions, and waste levels are acceptable.

The Orderlist Report contains sample placement information and sample cup volume requirements for all ordered tests. It is recommended that this report be referenced when loading samples into sample segments. When using Host Order Query, the Orderlist Report is not available. Refer to the AxSYM System Operations Manual, Section 5, for a description of the Host Order Query Option.

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 (RVs).
- Do not open the Interior Waste Door or the AxSYM Processing Center Cover unless 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 3rd Generation TSH Reagent Pack are removed from the Sampling Center to maximize the on-board reagent pack use. Store at 2-8°C.

SPECIMEN DILUTION PROCEDURES

Patient specimens with a TSH assay value exceeding 40.0 μIU/mL (HIGH RANGE, assay parameter 92) are flagged with the code "* 40.0 μIU/mL". To quantitate the concentration of these specimens, perform either the Automated Dilution Protocol or the Manual Dilution Protocol.

Automated Dilution Protocol

The Automated Dilution Protocol is provided to assist in quantitating test results greater than 40.0 μIU/mL and up to 200.0 μIU/mL. The AxSYM System performs a 1:5 dilution of the unknown specimen using one Reaction Vessel. The AxSYM System automatically calculates the concentration of the diluted specimen and reports the result.

If the assay is configured for auto dilution, include an additional 65 μL of sample volume in the sample container when ordering tests. Refer to the AxSYM System Operations Manual, Section 5, for additional information on ordering specimen dilutions.

Manual Dilution Protocol

Patient specimens with TSH concentrations reported as greater than 40.0 μIU/mL may be diluted using a suggested manual dilution of 1:10. Add 30 μL of the patient specimen to 270 μL of the AxSYM 3rd Generation TSH Standard Calibrator A (0.0 μIU/mL). The dilution should be performed so that the diluted test results read greater than the functional sensitivity of the assay (0.02 μIU/mL). The concentration reported by the AxSYM System must be multiplied by the manual dilution factor to obtain the final specimen concentration.

Final Specimen Concentration = Concentration x Dilution Factor

(Volume of Specimen + Manual Dilution Reagent) = Volume of Specimen

QUALITY CONTROL PROCEDURES

CALIBRATION

The AxSYM 3rd Generation TSH assay must be calibrated using a Standard Calibration (6-point) procedure.

Standard Calibration

To perform an AxSYM 3rd Generation TSH Standard Calibration, test the Standard Calibrators A, B, C, D, E, and F in duplicate. A single sample of all levels of TSH controls must be tested as a means of evaluating the assay calibration.

Once the AxSYM 3rd Generation TSH 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.
- Controls are out of range.
- The MEIA Optics Verification Update has been performed.

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, Appendix E, for an explanation of the corrective actions for the error code. Refer to the AxSYM System Operations Manual, Appendix E, for an explanation of the calibration validity parameters that may be used by the AxSYM System.
QUALITY CONTROL

The recommended control requirement for an AxSYM 3rd Generation TSH assay is a single sample of all TSH control levels tested once every 24 hours each day of use. Controls may be placed in any position in the Sample Carousel.

If the quality control procedures in your laboratory require more frequent use of controls to verify test results, follow those procedures.

To achieve maximum on-board reagent stability, more frequent use of controls may be required to monitor reagent performance within the same lot. Ensure that assay control values are within the concentration ranges specified in the package insert. Refer to the REAGENTS, CONTROLS section of this package insert for AxSYM 3rd Generation TSH Control ranges.

INDICATIONS OF INSTABILITY OR DETERIORATION OF REAGENTS

When a TSH control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results may be invalid and require retesting. Assay recalibration may be indicated. Refer to the AxSYM System Operations Manual, Section 10, for further troubleshooting information.

The AxSYM System has the capability to generate a Levey-Jennings plot of each panel member's quality control performance. Refer to the AxSYM System Operations Manual, Section 2, to display this plot and evaluate the relative pattern of results over time and their comparison to the normal range.


Precision was determined as described in the National Committee for Clinical Laboratory Standards (NCCLS) Protocol EP5-T2. Three buffer-based panel members (1, 2, and 3) and three processed human serum-based panel members (4, 5, and 6) were assayed, in replicates of two, at two separate times per day, for 20 days, using a single lot of reagents and a single calibration per instrument. Data from this study are summarized below.*

EXPECTED VALUES

Human serum and plasma specimens from 539 apparently healthy individuals were assayed using the AxSYM 3rd Generation TSH assay. The normal range obtained for TSH in serum was defined as 0.4 to 4.0 μIU/mL. The normal range obtained for TSH in plasma was defined as 0.4 to 4.0 μIU/mL. The normal range obtained for TSH in plasma was defined as 0.4 to 4.0 μIU/mL.

When a TSH control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results may be invalid and require retesting. Assay recalibration may be indicated. Refer to the AxSYM System Operations Manual, Section 10, for further troubleshooting information.

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, Appendix F, for further information.

QUALITY CONTROL WITH REGARD TO THE MUP SUBSTRATE BLANK is automatically determined by the instrument and checked under Assay Parameter 64, Max Intercept-Max MUP intercept, each time a test result is calculated. If the MUP intercept value is greater than the maximum allowable value, the result is invalid. The test request will be moved to the Exceptions List where it will appear with the message “1064 Invalid test result, intercept too high” and the calculated intercept value. Refer to the AxSYM System Operations Manual, Section 2, to display this plot and evaluate the relative pattern of results over time and their comparison to the normal range.

The AxSYM System has the capability to generate a Levey-Jennings plot of each panel member's quality control performance. Refer to the AxSYM System Operations Manual, Section 2, to display this plot and evaluate the relative pattern of results over time and their comparison to the normal range.

LIMITATIONS OF THE PROCEDURE

• For diagnostic purposes, the TSH results should be used in conjunction with other data, e.g., symptoms, results of other thyroid tests (e.g., Free T4), clinical impressions, etc.

• Suspected hyperthyroidism based on low or undetectable TSH levels should be confirmed with additional thyroid function testing along with other clinical information. Infrequently, TSH levels may appear elevated due to nonspecific protein binding.

• Pregnant women with hyperthyroidism (Graves' disease) may show elevated or depressed levels of TSH due to nonspecific protein binding.

• 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 which employ mouse monoclonal antibodies. These specimens should not be assayed with the AxSYM 3rd Generation TSH assay.

• Performance of this assay has not been established with neonatal specimens.

• Refer to the SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS section in this package insert for additional information.

EXPECTED VALUES

Human serum and plasma specimens from S39 apparently healthy individuals were evaluated using the AxSYM 3rd Generation TSH assay. The normal range obtained by testing these specimens is 0.47 to 4.64 μIU/mL (central 95%). It is recommended that each laboratory establish its own normal range, which may be unique to the population it serves depending upon geographical, patient, dietary, or environmental factors.

SPECIFIC PERFORMANCE CHARACTERISTICS

PRECISION

The AxSYM 3rd Gen TSH precision is < 8% (total CV) for concentrations in the range of panel members 1 and 2, and < 14.6% in the range of panel member 3. Precision was determined as described in the National Committee for Clinical Laboratory Standards (NCCLS) Protocol EPS-T2.20 Three buffer-based panel members (1, 2, and 3) and three processed human serum-based panel members (4, 5, and 6) were assayed, in replicates of two, at two separate times per day, for 20 days, using a single lot of reagents and a single calibration per instrument. Data from this study are summarized below.*
DILUTION LINEARITY

Dilution linearity was evaluated by serial dilution of four human serum specimens of known TSH concentrations, two within and two above the assay dynamic range, with AxSYM 3rd Generation TSH Standard Calibrator A (0.0 μIU/mL). For the two specimens above the assay dynamic range (specimens 3 and 4), the first dilution within the dynamic range was designated as the undiluted observed value.

<table>
<thead>
<tr>
<th>Specimen</th>
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<th>Observed Value (μIU/mL)</th>
<th>% Recovery</th>
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Sensitivity

The following data set exhibits a functional sensitivity of 0.012 μIU/mL and an upper 95% confidence limit of 0.015 μIU/mL. Therefore, the AxSYM 3rd Generation TSH assay meets the requirements of a 3rd generation TSH assay, which is defined as having an inter-assay CV of < 20% at < 0.02 μIU/mL TSH concentration.16 Functional sensitivity is defined as the lowest concentration of TSH that can be measured with an inter-assay CV of < 20%.21 It was measured by assaying single samples of a human serum panel which spans 0.005 to 0.150 μIU/mL. The assays were performed once a day over a period of time which approximates a clinically significant time period, the interval between thyroid patient visits.16 Functional sensitivity, therefore, represents the assay’s low end performance in actual laboratory use, rather than the lowest TSH concentration observable above zero, as defined by analytical sensitivity.

Representative data illustrating reagent performance was collected over 39 to 41 days from two lots of reagents tested on two AxSYM instruments with 15 to 18 test points per lot. The inter-assay %CVs were calculated, and plotted against the mean concentration. A multiplicative curve was fitted through the data, and the functional sensitivity was estimated as the concentration corresponding to the 20% CV on the fitted curve.
In this evaluation, serum and plasma specimens tested ranged from 0.028 to 39.522 μIU/mL with the AxSYM 3rd Generation TSH assay and 0.063 to 58.734 μIU/mL with the AxSYM Ultrasensitive hTSH II assay.

**BIBLIOGRAPHY**


For additional product information, please contact your local customer service organization.

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