Ferritin

Customer Service: Contact your local representative or find country specific contact information on www.abbottdiagnostics.com

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>REF</td>
<td>List Number</td>
</tr>
<tr>
<td>IVD</td>
<td>In Vitro Diagnostic Medical Device</td>
</tr>
<tr>
<td>LOT</td>
<td>Lot Number</td>
</tr>
<tr>
<td></td>
<td>Expiration Date</td>
</tr>
<tr>
<td>!</td>
<td>Caution</td>
</tr>
<tr>
<td>Store at 2-8°C</td>
<td></td>
</tr>
<tr>
<td>Store at 15-30°C</td>
<td></td>
</tr>
<tr>
<td>Manufacturer</td>
<td></td>
</tr>
<tr>
<td>STANDARD CAL A</td>
<td>Standard Calibrator (A-F)</td>
</tr>
<tr>
<td>CONTROL L</td>
<td>Control Low, Medium, High (L, M, H)</td>
</tr>
<tr>
<td>REAGENT PACK</td>
<td>Reagent Pack</td>
</tr>
<tr>
<td>REACTION VESSELS</td>
<td>Reaction Vessels</td>
</tr>
<tr>
<td>MATRIX CELLS</td>
<td>Matrix Cells</td>
</tr>
<tr>
<td>SAMPLE CUPS</td>
<td>Sample Cups</td>
</tr>
<tr>
<td>CONTAINS: AZIDE</td>
<td>Contains sodium azide. Contact with acids liberates very toxic gas. Consult instructions for use</td>
</tr>
</tbody>
</table>

See REAGENTS section for a full explanation of symbols used in reagent component naming.
hemosiderin, which most likely represents a form of denatured ferritin. In the form of ferritin. The remaining iron stores are contained in insoluble reticuloendothelial release of iron (e.g., anemia of chronic disease). Between depleted iron stores and conditions associated with defective does not distinguish iron deficiency as a progressive disease. Also, these studies have confirmed the direct relationship between serum ferritin concentration and iron stores in the body. Based on studies with normal volunteers, a concentration of 1 ng/mL of serum ferritin is equivalent to about 8 mg of stored iron. The mean serum ferritin concentration in human males is normally three times higher than in premenopausal females. The availability of sensitive methods for measuring serum ferritin has substantially advanced the ability to detect iron deficiency and excess body iron. In the United States, one study found iron deficiency anemia due to inadequate iron intake in 25% of infants, 6% of children, 15% of menstruating women and 30% of pregnant women. Since iron deficiency is present before the onset of anemia, detection of an iron depleted state is important for the control of nutritional anemia. The clinical assessment of iron stores has historically relied on the determination of serum iron, total iron-binding capacity (TIBC) and percent transferrin (ratio of serum iron and TIBC) or direct examination of bone marrow. The estimation of storable iron in the bone marrow is the traditional method for assessing body iron stores. This biopsy method provides a sensitive index of iron deficiency but has the disadvantage of being subjective and semiquantitative. Low hemoglobin concentration is the most readily available sign of anemia, but a significant fall in circulating hemoglobin cannot be detected until the final stage of iron deficiency anemia. Serum iron, TIBC and percent transferrin saturation do not distinguish iron deficiency as a progressive disease. Also, these measurements are affected by diurnal variation and may not discriminate between depleted iron stores and conditions associated with defective reticuloendothelial release of iron (e.g., anemia of chronic disease). Recent literature suggests that ferritin provides a more sensitive, specific and reliable measurement for determining iron deficiency at an early stage. In patients being given iron orally, serum ferritin measurements have been shown to be useful for monitoring the reaccumulation of iron stores and determining when therapy can be discontinued. In chronic inflammatory disorders, infections, and in chronic renal failure, there is a disproportionate increase in serum ferritin levels in relation to iron stores. The correlation of serum ferritin to body iron stores still exists, however, it is set at a higher level of serum ferritin. Numerous studies in the literature demonstrate the usefulness and necessity of serum ferritin measurements in combination with other parameters in determining the rate and degree of body iron overload in such disorders as thalassemia, sideroblastic anemia and in determining the response of patients treated with iron chelating agents. Specifically, the combined use of serum ferritin levels and mean corpuscular volume (MCV) has made differentiation between iron deficiency, beta-thalassemia trait and normal subjects possible at a very high level of accuracy. Serum ferritin measurements provide important clinical parameters for assessing the response to treatment with deferoxamine, an iron-chelating agent, in the treatment of thalassemia.
Solution 4 (Line Diluent) (8A46)
Preservatives: Sodium Azide and Antimicrobial Agents.

Solution 3 (Matrix Cell Wash) containing 0.3M Sodium Chloride in TRIS Buffer.

System operation.
More detailed discussion of the safety and handling precautions during installation procedures.

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.

Cleaning Solution containing 2% Tetraethylammonium Hydroxide (TEAH).

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CAUTION: This product contains human sourced and/or potentially infectious components. For a specific listing, refer to the REAGENTS section of this package insert. No known test method can offer complete assurance that products derived from human sources or inactivated microorganisms will not transmit infection. Therefore, all human sourced materials should be considered potentially infectious. It is recommended that these reagents and human specimens be handled in accordance with the OSHA Standard on Bloodborne Pathogens.20 Biosafety Level 21 or other appropriate biosafety practices22,23 should be used for materials that contain or are suspected of containing infectious agents.

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

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 use Reagent Packs beyond the expiration date or a maximum of 224 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

The AxSYM Ferritin Reagent Pack must be stored at 2-8°C (do not freeze). The AxSYM Ferritin Standard Calibrators and Controls must be stored at 2-8°C. The AxSYM Ferritin Reagent Pack, Standard Calibrators and Controls may be used immediately after removing them from the refrigerator. Standard Calibrators and Controls should be returned to 2-8°C storage immediately after use.

Reagents are stable until expiration date when stored and handled as directed.

The AxSYM Ferritin Reagent Pack may be on-board the AxSYM System for a maximum of 224 cumulative hours; for example 28 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.

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

ASSAY FILE INSTALLATION

The AxSYM Ferritin assay file must be installed on the AxSYM System from one of the following assay software disks, prior to performing Ferritin assays:

• 3DS2-02.

• 7GS3-01 or higher.

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

AxSYM Ferritin Assay Parameters

The default values for the visible assay parameters used for the AxSYM Ferritin assay are listed below. 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. However, some parameters that contain a (>) symbol may not be editable if there are no additional options. 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

1 Long Assay Name (English): Ferritin
2 Abbrev Assay Name (English): Ferritin
3D52-02.
11 Assay Number: 3Z1
3D52-02.
12 Assay Version: *
13 Calibration Version: *
14 Assay File Revision: *
15 Assay Enabled > ON
17 Assay Type: MEIA
18 Standard Cal Reps > 2
21 Cal A Concentration: 0.00
22 Cal B Concentration: 10.00
23 Cal C Concentration: 50.00
24 Cal D Concentration: 250.00
25 Cal E Concentration: 500.00
26 Cal F Concentration: 1000.00
35 Default Dilution Protocol > UNDILUTED
44 Default Calibration Method > Standard Cal
45 Selected Result Concentration Units > ng/mL
46 Selected Result Decimal Places > 2
64 Max Intercept-Max MUP intercept: *
65 Min Intercept-Min MUP intercept: *

INSTRUMENT PROCEDURE

ASSAY FILE INSTALLATION

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• 3DS2-02.

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24 Cal D Concentration: 250.00
25 Cal E Concentration: 500.00
26 Cal F Concentration: 1000.00
35 Default Dilution Protocol > UNDILUTED
44 Default Calibration Method > Standard Cal
45 Selected Result Concentration Units > ng/mL
46 Selected Result Decimal Places > 2
64 Max Intercept-Max MUP intercept: *
65 Min Intercept-Min MUP intercept: *
To obtain the recommended volume requirements for the AxSYM Ferritin Standard Calibrators and Controls, hold the bottles vertically and dispense 5 drops of each Calibrator or 4 drops of each Control into each respective sample cup. If the assay is configured for Auto Retest/Auto Dilution the additional sample volume needed for the retest will not be displayed on the Order screen at the time the test(s) is (are) ordered. Therefore, the total sample volume should include an additional 81 μL of sample. Refer to the AxSYM System Operations Manual, Section 2, for details on Automatic Sample Retest Configuration.

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 FERRITIN PROCEDURE**

**Materials Provided**
- 7K45-20 AxSYM Ferritin Reagent Kit, containing:
  - AxSYM Ferritin REAGENT PACK
  - 100 REACTION VESSELS
  - 100 MATRIX CELLS

**Materials Required But Not Provided**
- AxSYM System
- 7K45-01 AxSYM Ferritin Standard Calibrators
- 7K45-10 AxSYM Ferritin Controls
- 8A47-04 SOLUTION 1 MUP
- 8A81-04 SOLUTION 2 MATRIX CELL WASH
- 8A46 SOLUTION 3 LINE DI LUTION
- 9A35-05 AxSYM PROBE CLEANING SOLUTION
- 8A76-01 SAMPLE CUPS
- 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 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, Ordering Patient Samples, 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 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 Ferritin Reagent Pack are removed from the Sampling Center to maximize the on-board reagent pack use. Store at 2-8°C.

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**Assay Parameters**

<table>
<thead>
<tr>
<th>Assay Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Min Rate-Rate</td>
<td>100 μL</td>
</tr>
<tr>
<td>Max Rate-Rate</td>
<td>0.00 μL</td>
</tr>
<tr>
<td>Min correlation coefficient for high rates</td>
<td>*</td>
</tr>
<tr>
<td>DILUTION</td>
<td>0.00 μL</td>
</tr>
<tr>
<td>MUP</td>
<td>0.00 μL</td>
</tr>
<tr>
<td>Low Limit-Normal/Therapeutic Range</td>
<td>0.00 μL</td>
</tr>
<tr>
<td>High Limit-Normal/Therapeutic Range</td>
<td>0.00 μL</td>
</tr>
</tbody>
</table>

---

**Sample Volume**

The sample volume required to perform a single ferritin test on the AxSYM System varies depending on the type of sample container used. For sample cups, 150 μL is required unless the test is performed as STAT. The minimum sample volume required for a STAT test is 100 μL. For every additional ferritin test performed (ROUTINE and STAT) from the same sample container, an additional 50 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 and printed on the Orderlist Report. When using Host Order Query, the Order screen information and Orderlist Report are not available. Refer to the AxSYM System Operations Manual, Section 5, Ordering Patient Samples, for a description of the Host Order Query Option.
QUALITY CONTROL PROCEDURES

Calibration

The AxSYM Ferritin Assay must be calibrated using a Standard Calibration (6-point) procedure.

Standard Calibration

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

Once the AxSYM Ferritin 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.

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. 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 Ferritin Assay is a single sample of all ferritin 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 Ferritin Control ranges.

Indications of Instability or Deterioration of Reagents

When a 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, Subsection: Observed Problems, for further troubleshooting information.

The AxSYM System has a capability to generate a Levey-Jennings plot of each assay's quality control performance. Refer to the AxSYM System Operations Manual, Section 5. At the discretion of the laboratory, selected quality control rules may be applied to the quality control data.

Fluorescence Background Acceptance Criteria

Quality Control with regards 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 10, when this error message is obtained.

Refer to the AxSYM System Operations Manual, Section 2, for further information on this parameter.

RESULTS

AxSYM Ferritin utilizes a point-to-point reduction method to generate a Standard calibration curve.

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 AxSYM System Operations Manual, Sections 1 and 2.

LIMITATIONS OF THE PROCEDURE

- For diagnostic purposes, the AxSYM Ferritin 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 (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 Ferritin assay.

Refer to the SAMPLE COLLECTION AND PREPARATION FOR ANALYSIS section in this package insert.

EXPECTED VALUES

Evaluation of serum specimens from 99 normal males, 97 premenopausal, and 99 postmenopausal females with the AxSYM Ferritin assay yielded the following results.

<table>
<thead>
<tr>
<th>Normal Range Summary</th>
<th>No. of Subjects</th>
<th>Range* (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Males (18-30 yrs. of age)</td>
<td>53</td>
<td>18.7 - 323.0</td>
</tr>
<tr>
<td>Adult Males (31-60 yrs. of age)</td>
<td>46</td>
<td>16.4 - 293.9</td>
</tr>
<tr>
<td>Adult Females (Premenopausal)</td>
<td>97</td>
<td>6.9 - 282.5</td>
</tr>
<tr>
<td>Adult Females (Postmenopausal)</td>
<td>99</td>
<td>14.0 - 233.1</td>
</tr>
</tbody>
</table>

* Non-parametric estimate of the 95% confidence interval.

These individuals were determined to be normal based on test results for blood count, transaminases, gamma GT, or erythrocyte sedimentation rate. Pregnant women were excluded from the premenopausal group. It is recommended that each laboratory establish its own normal range appropriate to the population it serves.

Ferritin levels below 10 ng/mL have been reported as indicative of iron deficiency anemia. There are patients with iron deficiency anemia who have elevated or normal ferritin levels because of other causes, such as, hepatocellular disease or iron therapy. Abnormally HIGH ferritin levels (up to 50,000 ng/mL), can be determined with the AxSYM Ferritin assay without experiencing a high-dose hook effect.

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The AxSYM Ferritin assay is designed to have a total run precision of ≤ 9 total %CV for concentrations within the ferritin low, medium, and high control ranges.

Precision was determined as described in Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) protocol EPS-T2. A three member buffered protein 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 in the following tables.
**assay and the resulting percent recovery was calculated.** The concentration of ferritin was determined using the AxSYM Ferritin kit. The AxSYM Ferritin assay is designed to have a mean recovery of 100 ± 10% when analyzing specimens spiked with known amounts of ferritin. These data represent a correlation coefficient (r) of ≥ 0.95 within the range of 1 - 1000 ng/mL when compared to the IMx Ferritin assay.

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

### Table 1: Comparison of AxSYM Ferritin vs. IMx Ferritin

<table>
<thead>
<tr>
<th>Method</th>
<th>Number of Observations</th>
<th>Intercept</th>
<th>Slope</th>
<th>Correlation Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Least Squares</td>
<td>198</td>
<td>-1.12</td>
<td>1.02</td>
<td>0.992</td>
</tr>
<tr>
<td>Linear Regression</td>
<td>198</td>
<td>0.36</td>
<td>1.01</td>
<td>0.992</td>
</tr>
<tr>
<td>Passing-Bablok Linear Regression</td>
<td>198</td>
<td>0.36</td>
<td>1.01</td>
<td>0.992</td>
</tr>
</tbody>
</table>

* Representative data; results in individual laboratories may vary from these data.

### Recovery

The AxSYM Ferritin assay is designed to have a mean recovery of 100 ± 10% when analyzing specimens spiked with known amounts of ferritin. Known concentrations of ferritin were added to 5 human serum samples. The concentration of ferritin was determined using the AxSYM Ferritin assay and the resulting percent recovery was calculated.**

**Abbreviations:**
- Ferritin Value Obtained (ng/mL) – Ferritin Value Obtained (ng/mL) - Endogenous Level (ng/mL) x 100
- Ferritin Added (ng/mL) – Ferritin Added (ng/mL)
- Average Percent Recovery: 93.1%

**Notes:**
- Passing-Bablok Linear Regression is a non-parametric method.
- A linear regression method with no assumptions regarding the distribution of the samples and measurement errors.28

**BIBLIOGRAPHY**