
Caution For U.S.A. only, Federal law restricts this device to sale and distribution by or on the order of a physician, or to a clinical laboratory; and use is restricted to by or on the order of a physician.

Warning The concentration of CA 15-3 antigen in a given specimen determined with assays from different manufacturers can vary due to differences in assay methods and reagent specificity. The results reported by the laboratory to the physician must include the identity of the CA 15-3 antigen assay used. Values obtained with different assay methods cannot be used interchangeably. If, in the course of monitoring a patient, the assay method used for determining CA 15-3 antigen values is changed, additional sequential testing should be carried out to confirm baseline values.

Intended Use The Access BR Monitor assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of CA 15-3 antigen levels in human serum and plasma (heparin) using the Access Immunoassay Systems. This device is indicated for use in the measurement of CA 15-3 antigen to aid in the management of breast cancer patients. Serial testing for CA 15-3 antigen concentrations should be used in conjunction with other clinical methods for monitoring breast cancer.

Summary and Explanation The CA 15-3 antigen is an epitope on a large mucin-like glycoprotein, which is a product of MUC1.^{1,2} Mucins, present in normal glandular epithelia of various organs, serve to protect and lubricate surrounding cells.^{1,2,3} In breast cancer, the MUC1 mucin becomes aberrantly glycosylated, overexpressed and released into circulation. Once released into circulation, it may be detected at elevated levels.^{1,2,3,4}

CA 15-3 antigen levels are elevated in many patients with epithelial breast carcinoma. Elevated levels of CA 15-3 antigen may also be present in those patients with lung, ovarian, pancreatic, and colorectal cancers, as well as non-malignant conditions including benign breast and liver disease, cirrhosis, and hepatitis.^{2,5,6}

In the United States, breast cancer is a leading cause of cancer death in women, second to lung cancer.⁷ In the world, breast cancer has become one of the most common cancers affecting 1 in 10 women.⁵

CA 15-3 antigen, has become a widely recognized breast cancer marker^{1,2} and has been shown to be more sensitive than CEA in detecting recurrence of breast cancer.^{6,8} Increasing CA 15-3 antigen levels may be representative of disease progression, where as, decreasing antigen levels may be associated with disease regression.⁸

The Access BR Monitor assay is not recommended as a screening tool. A value below the cutoff limit does not indicate the absence of breast cancer. Other clinically acceptable tests and procedures should also be considered in the monitoring of breast cancer and good patient management.

Principles of the Procedure The Access BR Monitor assay is a two-site immunoenzymatic ("sandwich") assay. A sample is added to a reaction vessel along with mouse monoclonal anti-CA 15-3 antigen alkaline phosphatase conjugate and paramagnetic particles coated with a second mouse monoclonal

anti-CA 15-3 antigen antibody. The CA 15-3 antigen in the sample binds to the immobilized monoclonal anti-CA 15-3 antigen on the solid phase, while the conjugate antibody reacts with a different antigenic site on the CA 15-3 antigen molecule. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Then, the chemiluminescent substrate Lumi-Phos* 530 is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is directly proportional to the concentration of CA 15-3 antigen in the sample. The amount of analyte in the sample is determined from a stored, multi-point calibration curve.

Product Information

Access BR Monitor Reagent Pack

Cat. No. 387620: 100 determinations, 2 packs, 50 tests/pack

- Provided ready to use.
- Store upright and refrigerate at 2 to 10°C.
- Refrigerate at 2 to 10°C for a minimum of two hours before use on the instrument.
- Stable until the expiration date stated on the label when stored at 2 to 10°C.
- Stable at 2 to 10°C for 56 days after initial use.
- Signs of possible deterioration are a broken elastomeric layer on the pack or control values out of range.
- If the reagent pack is damaged (i.e., broken elastomer), discard the pack.
- All antisera are polyclonal unless otherwise indicated.

R1a:	Paramagnetic particles, coated with goat anti-biotin antibodies, biotinylated anti-CA 15-3 antigen mouse monoclonal antibodies, bovine serum albumin, < 0.1% sodium azide and 0.1% ProClin** 300.
R1b:	Mouse monoclonal anti-CA 15-3 antigen-alkaline phosphatase (bovine) conjugate, bovine serum albumin, < 0.1% sodium azide, 0.25% ProClin 300.
R1c:	Buffered protein solution (bovine, goat, mouse), < 0.1% sodium azide, 0.1% ProClin 300.

Warnings and Precautions

- For *in vitro* diagnostic use.
- Patient samples and blood-derived products may be routinely processed with minimum risk using the procedure described. However, handle these products as potentially infectious according to universal precautions and good clinical laboratory practices, regardless of their origin, treatment, or prior certification. Use an appropriate disinfectant for decontamination. Store and dispose of these materials and their containers in accordance with local regulations and guidelines.
- Human source material used in the preparation of the reagent has been tested and found negative or non-reactive for Hepatitis B, Hepatitis C (HCV), and Human Immunodeficiency Virus (HIV-1 and HIV-2). Because no known test method can offer complete assurance that infectious agents are absent, handle reagents and patient samples as if capable of transmitting infectious disease.⁹
- Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. On disposal of liquids, flush with a large volume of water to prevent azide build-up.¹⁰
- Xi. Irritant: 0.25% ProClin 300.



R 43: May cause sensitization by skin contact.

S 28-37: After contact with skin, wash immediately with plenty of soap and water. Wear suitable gloves.

- The Material Safety Data Sheet (MSDS) is available upon request.

**Specimen
Collection and
Preparation**

1. Serum and plasma (heparin) are the recommended samples.
 2. Observe the following recommendations for handling, processing, and storing blood samples:¹¹
 - Collect all blood samples observing routine precautions for venipuncture.
 - Allow serum samples to clot completely before centrifugation.
 - Keep tubes stoppered at all times.
 - Within two hours after centrifugation, transfer at least 500 µL of cell-free sample to a storage tube. Tightly stopper the tube immediately.
 - Store samples tightly stoppered at room temperature (15 to 30°C) for no longer than eight hours.
 - If the assay will not be completed within eight hours, refrigerate the samples at 2 to 8°C.
 - If the assay will not be completed within 48 hours, or for shipment of samples, freeze at -20°C or colder.
 - Thaw samples only once.
 3. Use the following guidelines when preparing specimens:
 - Ensure residual fibrin and cellular matter has been removed prior to analysis.
 - Follow blood collection tube manufacturer's recommendations for centrifugation.
 4. Each laboratory should determine the acceptability of its own blood collection tubes and serum separation products. Variations in these products may exist between manufacturers and, at times, from lot-to-lot.
 5. Avoid assaying lipemic and/or hemolyzed samples.
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**Materials
Provided**

- R1 Access BR Monitor Reagent Packs
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**Materials
Required But
Not Provided**

1. Access BR Monitor Calibrators
Provided at zero and approximately 10, 50, 100, 500 and 1000 U/mL.
Cat. No. 387647
 2. Quality Control (QC) materials: commercial control material
 3. Access Sample Diluent A
Vial Cat. No. 81908
Diluent Pack Cat. No. A79783 (For use with the UniCel DxI system onboard dilution feature.)
 4. Access Substrate
Cat. No. 81906
 5. **Access, Access 2, SYNCHRON LXi:**
Access Wash Buffer II, Cat. No. A16792
UniCel DxI:
UniCel DxI Wash Buffer II, Cat. No. A16793
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**Procedural
Comments**

1. Refer to the appropriate system manuals and/or Help system for a specific description of installation, start-up, principles of operation, system performance characteristics, operating instructions, calibration procedures, operational limitations and precautions, hazards, maintenance, and troubleshooting.
 2. Mix contents of new (unpunctured) reagent packs by gently inverting pack several times before loading on the instrument. Do not invert open (punctured) packs.
 3. Use ten (10) µL of sample for each determination in addition to the sample container and system dead volumes. Use fifty (50) µL of sample in addition to the sample container and system dead volumes for each determination run with the DxI system onboard dilution feature. Refer to the appropriate system manuals and/or Help system for the minimum sample volume required.
 4. The system default unit of measure for sample results is U/mL.
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Procedure Refer to the appropriate system manuals and/or Help system for information on managing samples, configuring tests, requesting tests, and reviewing test results.

Calibration Details An active calibration curve is required for all tests. For the Access BR Monitor assay, calibration is required every 56 days. Refer to the appropriate system manuals and/or Help system for information on calibration theory, configuring calibrators, calibrator test request entry, and reviewing calibration data.

Quality Control Quality control materials simulate the characteristics of patient samples and are essential for monitoring the system performance of immunochemical assays. Because samples can be processed at any time in a “random access” format rather than a “batch” format, quality control materials should be included in each 24-hour time period.¹² Include commercially available quality control materials that cover at least two levels of analyte. More frequent use of controls or the use of additional controls is left to the discretion of the user based on good laboratory practices or laboratory accreditation requirements and applicable laws. Follow manufacturer’s instructions for reconstitution and storage. Each laboratory should establish mean values and acceptable ranges to assure proper performance. Quality control results that do not fall within acceptable ranges may indicate invalid test results. Examine all test results generated since obtaining the last acceptable quality control test point for this analyte. Refer to the appropriate system manuals and/or Help system for information about reviewing quality control results.

Results Patient test results are determined automatically by the system software using a weighted four parameter logistic curve (4PLC). The amount of analyte in the sample is determined from the measured light production by means of the stored calibration data. Patient test results can be reviewed using the appropriate screen. Refer to the appropriate system manuals and/or Help system for complete instructions on reviewing sample results.

- Limitations of the Procedure**
1. Samples can be accurately measured within the analytic range of the lower limit of detection and the highest calibrator value approximately (0.5–1000 U/mL).
 - If a sample contains less than the lower limit of detection for the assay, report the results as less than that value (i.e., < 0.5 U/mL). When the DxI system onboard dilution feature is used, the system will report results as less than 850 U/mL.
 - If a sample contains more than the stated value of the highest Access BR Monitor Calibrator (S5), report the result as greater than that value (i.e., >1000 U/mL). Alternatively, dilute one volume of sample with nine volumes of Access Sample Diluent A. Refer to the appropriate system manuals and/or Help system for instructions on entering a sample dilution in a test request. The system reports the results adjusted for the dilution.
The DxI system onboard dilution feature automates the dilution process, using one volume of sample with nine volumes of Access Sample Diluent A, allowing samples to be quantitated up to approximately 10,000 U/mL. The system reports the results adjusted for the dilution.
 2. For assays employing antibodies, the possibility exists for interference by heterophile antibodies in the patient sample. Patients who have been regularly exposed to animals or have received immunotherapy or diagnostic procedures utilizing immunoglobulins or immunoglobulin fragments may produce antibodies, e.g. HAMA, that interfere with immunoassays. Additionally, other heterophile antibodies such as human anti-goat antibodies may be present in patient samples.^{13,14}
Such interfering antibodies may cause erroneous results. Carefully evaluate the results of patients suspected of having these antibodies.
 3. The Access BR Monitor results should be interpreted in light of the total clinical presentation of the patient, including: symptoms, clinical history, data from additional tests, and other appropriate information.

4. Serum or plasma CA 15-3 antigen concentrations should not be interpreted as absolute evidence for the presence or absence of cancer. Elevated concentrations may be observed in the serum or plasma of patients with benign conditions, pregnancy^{15,16} or other non-cancer disorders, as well as in breast cancer and other malignant diseases. The Access BR Monitor Assay should not be used as a cancer screening test.
5. The Access BR Monitor assay does not demonstrate any “hook” effect up to 30,000 U/mL.

Expected Values

1. Each laboratory should establish its own reference ranges to assure proper representation of specific populations.
2. The distribution of Access BR Monitor results, presented below was determined from a total of 1,244 serum samples from apparently healthy females and females with non-malignant and malignant conditions. Results from 43 apparently healthy males and 51 males with prostate cancer are included in the table.

Subject Category	Number of Subjects	0–31.3 U/mL	31.4–60 U/mL	60.1–120 U/mL	> 120 U/mL
Apparently Healthy					
Females < 50 years	152	152	0	0	0
Females ≥ 50 years	152	151	1	0	0
Males	43	43	0	0	0
Malignant Conditions					
Breast Cancer					
Stage I	48	48	0	0	0
Stage II	78	76	2	0	0
Stage III	38	29	4	3	2
Stage IV	40	21	5	4	10
Cervical	24	22	1	0	1
Colon	18	17	1	0	0
Esophageal	9	9	0	0	0
Endometrial	6	6	0	0	0
Fallopian tube	3	2	0	0	1
Gastric/Stomach	43	40	3	0	0
Liver	55	50	2	1	2
Lung	29	22	6	0	1
Pancreatic	14	11	1	1	1
Prostate (males)	51	46	4	1	0
Ovarian	51	40	6	5	0
Vaginal/Vulva	11	10	1	0	0
Uterine	18	13	4	1	0
Non-Malignant Conditions					
Breast	79	76	3	0	0
Colon	43	42	1	0	0
Cystitis	26	23	3	0	0
Gastric/Stomach	37	31	3	3	0
Kidney/Renal Failure	49	45	4	0	0
Liver	45	44	1	0	0
Lung	40	40	0	0	0
Ovarian	25	24	1	0	0
Pelvic Inflammatory disease	23	22	1	0	0
Pregnancy	67	67	0	0	0
Uterine Fibroids	21	20	1	0	0

Clinical Performance

Serial samples from monitored subjects with known disease status (total of 140 samples) were obtained from 36 females (ages ranging from 36 to 84 years) who were diagnosed with breast cancer (stages II to IV). These subjects were monitored over the course of disease, ranging from 4 months to 41 months follow-up. These subjects may have undergone surgery, hormonal therapy, chemotherapy, and/or radiation therapy during the course of disease management. The method(s) used to determine disease status at sample draw date included: mammography, biopsy, physical exam, x-rays, CAT scan, ultrasound, isotope scan, CA 15-3 measurements, and/or MRI. Disease status is based on one or more clinical diagnostic modalities at the time for each serial blood draw. The determination of disease status was made by the clinician.

Samples from this previously described population of subjects were used for the analyses presented below:

- 1) Percent positive agreement and percent negative agreement (relative to an automated commercially available CA 15-3 assay);
- 2) Clinical sensitivity and specificity (based on disease status at time of serial blood draw).

Percent Positive Agreement and Percent Negative Agreement

Percent positive agreement and percent negative agreement were calculated for the Access BR Monitor versus another automated commercially available assay. In this study percent positive agreement and percent negative agreement calculations were based on the 31.3 U/mL upper reference limit (URL) for both assays. The analyses were based on 140 samples from 36 subjects originally diagnosed with breast cancer (stages II to IV) and at various stages of the disease. Based on the 140 samples from the 36 breast cancer subjects, the percent positive agreement and percent negative agreement were 83.8% and 98.5%, respectively. The percent total agreement between the two assays is 90.7%.

Clinical Sensitivity and Clinical Specificity

In this study, clinical sensitivity and clinical specificity were based on the 31.3 U/mL URL. Clinical sensitivity is calculated based on a total of 44 serum samples from 25 females originally diagnosed with breast cancer (stages II to IV) with disease status of “progression” at the time of sample draw date. Clinical specificity is calculated based on a total of 20 samples from 11 females originally diagnosed with breast cancer (stages II to IV) with disease status of “No Evidence of Disease” at the time of sample draw date. Based on these two populations, the clinical sensitivity and specificity for the Access BR Monitor assay, based on the 31.3 U/mL URL, were 70.5% and 90.0%, respectively. Comparable results, 75% and 85% for clinical sensitivity and clinical specificity, were obtained with another automated commercially available assay.

Monitoring of Patients Diagnosed with Breast Cancer

The Least Significant %Change (LS %Change) represents the minimum magnitude change between two serial CA 15-3 antigen measurements that could not be attributed to assay variation or noise. Based on regression models, a 25% LS %Change was selected to cover the imprecision across the range of Access BR Monitor concentrations. The LS %Change corresponds to 2.5 times the %CV (coefficient of variation) for imprecision, for the Access BR Monitor assay.

The effectiveness of CA 15-3 antigen measurements as an aid in monitoring disease status in patients diagnosed with breast cancer was determined by assessing changes in CA 15-3 antigen levels in serial sets (pairs) with change in disease status. The 36 breast cancer subjects, from the serial monitoring study, were analyzed using one serial set (two sequential visits per set) per subject. In this evaluation, disease status was classified as “Progression” or “No Progression”, with “No Progression” consisting of “Stable/No Evidence of Disease (NED)” and “Responding” between two consecutive serial draws. The results from these analyses, on a per patient basis, are presented below.

**%Change in CA 15-3 Antigen Concentrations vs. Clinical Status
Based on 25% Least Significant %Change (Per Patient Basis)**

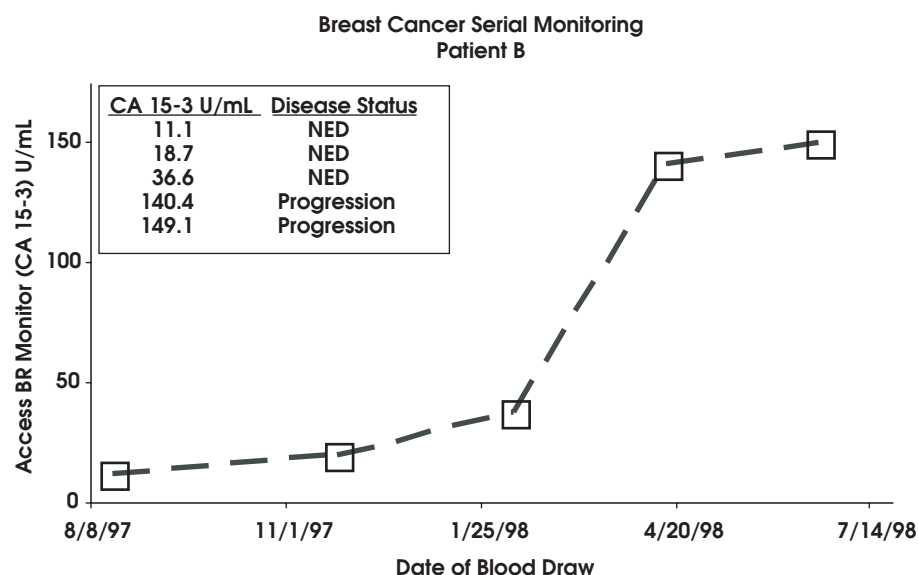
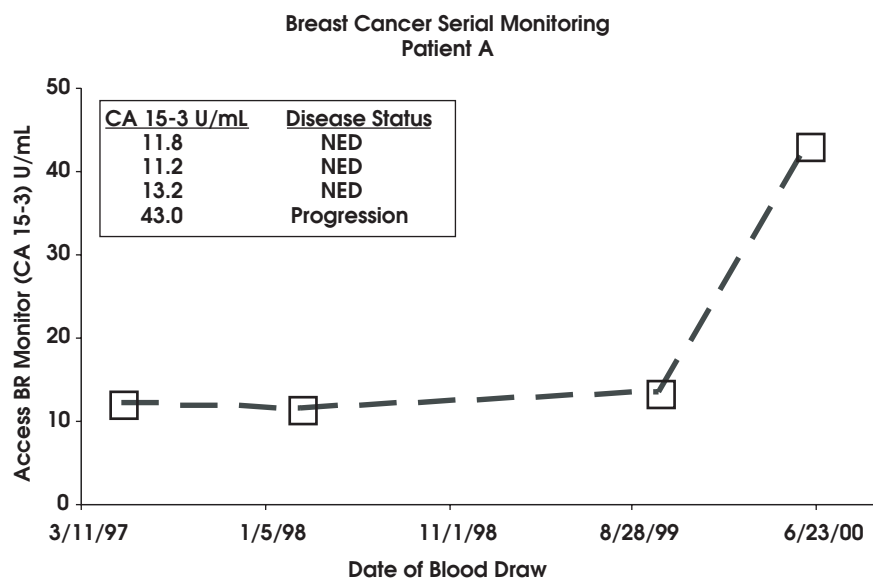
Access BR Monitor	Change in Clinical Status		Total
Change in CA 15-3 Antigen	Progression	No Progression	
Significant Change > 25%	14	1	15
No Change ≤ 25%	8	13	21
Total	22	14	36
Access BR Monitor		95% Confidence Interval	
Positive Concordance (Sensitivity)	63.6%	43.0%	80.3%
Negative Concordance (Specificity)	92.9%	68.5%	98.7%
Total Concordance	75.0%	58.9%	86.3%

The effectiveness of CA 15-3 antigen measurements to aid in the management of breast cancer patients was also further determined by assessing changes in CA 15-3 antigen levels in serial sets (sequential visit pairs) with changes in disease status. Samples from 36 patients from the serial monitoring study, for a total of 103 serial sets (sequential visit pairs), were further analyzed for %Change in CA 15-3 antigen concentrations across serial sets and disease status. In this evaluation disease status, between consecutive serial draws, was classified as “Progression” or “No Progression”, with “No Progression” consisting of “Stable/No Evidence of Disease (NED)” and “Responding”. The distribution of results across the two disease classifications relative to the 25% LS %Change, on a per sample basis, are presented below for the Access BR Monitor assay.

**%Change in CA 15-3 Antigen Concentrations vs. Clinical Status
Based on 25% Least Significant %Change (Per Visit Basis)**

Access BR Monitor	Change in Clinical Status		Total
Change in CA 15-3 Antigen	Progression	No Progression	
Significant Change > 25%	18	25	43
No Change ≤ 25%	16	44	60
Total	34	69	103
Access BR Monitor		95% Confidence Interval	
Positive Concordance (Sensitivity)	52.9%	36.7% to 68.6%	
Negative Concordance (Specificity)	63.8%	52.0% to 74.1%	
Total Concordance	60.2%	50.5% to 69.1%	

Below are two examples showing serial monitoring profiles for the Access BR Monitor CA 15-3 antigen values and the clinical status.



Specific Performance Characteristics

Methods Comparison

A comparison of 435 values using the Access BR Monitor assay on the Access Immunoassay system and a commercially available immunoassay kit gave the following statistical data using Deming calculations:

n	Range of Observations (U/mL)	Intercept (U/mL)	Slope	Correlation Coefficient (r)
435	0-250	1.92	0.82	0.91

Dilution Recovery (Linearity)

Multiple dilutions of 3 samples containing various CA 15-3 antigen levels with Access Sample Diluent A resulted in the following data:

Sample 1	Expected Concentration (U/mL)	Determined Concentration (U/mL)	Recovery (%)
Neat	1005.2	–	100.0
1:2	502.6	459.7	91.5
1:4	251.3	229.4	91.3
1:8	125.7	109.5	87.1
1:20	50.3	44.0	87.5
1:40	25.1	22.8	90.8
1:80	12.6	10.7	84.9
Mean % Recovery			88.9

Sample 2	Expected Concentration (U/mL)	Determined Concentration (U/mL)	Recovery (%)
Neat	451.6	–	100.0
1:2	225.8	231.4	102.5
1:4	112.9	116.9	103.5
1:8	56.5	55.7	98.6
1:20	22.6	23.1	102.2
1:40	11.3	13.1	115.9
1:80	5.6	6.3	112.5
Mean % Recovery			105.9

Sample 3	Expected Concentration (U/mL)	Determined Concentration (U/mL)	Recovery (%)
Neat	403.8	–	100.0
1:2	201.9	200.1	99.1
1:4	100.9	98.2	97.3
1:8	50.5	50.4	99.8
1:20	20.2	20.1	99.5
1:40	10.1	11.2	110.9
1:80	5.1	5.9	115.7
Mean % Recovery			103.7

Imprecision

This assay exhibits total imprecision of $\leq 10\%$ for concentrations between 15 and 500 U/mL, and $\leq 12\%$ for concentrations greater than 500 U/mL. One study, using commercially available human serum based control material generating a total of 20 assays, 2 replicates per assay, over 20 days provided the following data, analyzed via analysis of variance (ANOVA).^{17,18}

Sample	Grand Mean (n=40) (U/mL)	Within Run (%CV)	Between Run (%CV)	Total Imprecision (%CV)
Level 1	14.7	1.4	1.6	2.1
Level 2	98.0	2.2	4.1	4.6
Level 3	243.2	1.5	2.2	2.6
Level 4	661.8	1.9	1.8	2.6

Analytical Specificity/Interferences

Samples containing up to 500 mg/dL hemoglobin, 40 mg/dL bilirubin, 3000 mg/dL triglyceride (triolein) or 6 g/dL protein (human serum albumin) do not affect the concentration of CA 15-3 antigen assayed.

The following table describes the cross-reactivity of the assay with common chemotherapeutic agents and other potential interferents.

Substance	Concentration Added	Expected (U/mL)	Observed (U/mL)	Mean % Recovery
5-Fluorouracil	500 µg/mL	25.3	25.7	101.8
Acetaminophen (Tylenol)	200 µg/mL	42.7	43.2	101.3
Amethopterin (Methotrexate)	250 µg/mL	33.5	32.1	95.7
Aspirin (Acetylsalicylic Acid)	500 µg/mL	42.7	42.9	100.4
B-Estradiol	10 µg/mL	41.4	42.3	102.4
Cis-Platinum (II) Diammine Dichloride (Cisplatin)	2,000 µg/mL	38.2	38.3	100.3
Cyclophosphamide	1,000 µg/mL	40.8	39.4	96.6
Doxorubicin Hydrochloride	100 µg/mL	41.5	41.5	100.0
Estrone 3-Sulfate, Na salt	10 µg/mL	41.1	41.1	100.1
Folinic Acid, Ca salt (Leucovorin)	200 µg/mL	40.5	41.4	102.2
Heparin, Li	8 U/mL	33.3	32.7	98.4
Heparin, Na	8 U/mL	34.8	35.1	101.0
Ibuprofen	400 µg/mL	42.7	43.5	101.9
Megesterol Acetate	40 µg/mL	38.2	40.8	106.8
Mitomycin C	15 µg/mL	41.1	40.5	98.4
Mitoxantrone Hydrochloride (Novantrone)	2 µg/mL	43.0	43.7	101.7
*Multivitamin	1:20	33.6	33.2	98.9
Paclitaxel	5 µg/mL	43.0	42.3	98.5
Tamoxifen Citrate	100 µg/mL	43.5	42.9	98.6
Testosterone	40 µg/mL	43.5	43.5	100.0
Vinblastine Sulfate	2 µg/mL	41.1	43.1	104.9
Vincristine Sulfate	2 µg/mL	41.1	43.2	105.0
Warfarin	1.5 mg/mL	38.4	37.4	97.5

* Multivitamin substances were at the following concentrations: 8.33 IU/mL Vitamin A, 200 µg/mL Vitamin C, 1.3 IU/mL Vitamin D, 0.1 IU/mL Vitamin E, 5 µg/mL Thiamin (B1), 5.67 µg/mL Riboflavin (B2), 66.7 µg/mL Niacin, 6.67 µg/mL Vitamin B6, 20 ng/mL Vitamin B12 and 1 µg/mL Biotin.

Analytical Sensitivity

The lowest detectable level of CA 15-3 antigen distinguishable from zero (Access BR Monitor Calibrator S0) with 95% confidence is < 0.5 U/mL. This value is determined by processing a complete six point calibration curve, controls, and 10 replicates of the zero calibrator in multiple (10) assays. The analytical sensitivity value is calculated from the curve at the point that is two standard deviations from the fitted zero calibrator signal.

BR MONITOR CALIBRATORS

REF 387647

Caution For U.S.A. only, Federal law restricts this device to sale and distribution by or on the order of a physician, or to a clinical laboratory; and use is restricted to by or on the order of a physician.

Warning The concentration of CA 15-3 antigen in a given specimen determined with assays from different manufacturers can vary due to differences in assay methods and reagent specificity. The results reported by the laboratory to the physician must include the identity of the CA 15-3 antigen assay used. Values obtained with different assay methods cannot be used interchangeably. If, in the course of monitoring a patient, the assay method used for determining CA 15-3 antigen values is changed, additional sequential testing should be carried out to confirm baseline values.

Intended Use The Access BR Monitor Calibrators are intended to calibrate the Access BR Monitor assay for the quantitative determination of CA 15-3 antigen levels in human serum and plasma using the Access Immunoassay Systems.

Summary and Explanation Quantitative assay calibration is the process by which samples with known analyte concentrations (i.e., assay calibrators) are tested like patient samples to measure the response. The mathematical relationship between the measured responses and the known analyte concentrations establishes the calibration curve. This mathematical relationship, or calibration curve, is used to convert RLU (Relative Light Unit) measurements of patient samples to specific quantitative analyte concentrations.

Traceability The measurand (analyte) in the Access BR Monitor Calibrators is traceable to the manufacturer's working calibrators. Traceability process is based on EN ISO 17511.

The assigned values were established using representative samples from this lot of calibrator and are specific to the assay methodologies of the Access reagents. Values assigned by other methodologies may be different. Such differences, if present, may be caused by inter-method bias.

Product Information **Access BR Monitor Calibrators**
Cat. No. 387647: S0–S5, 1.5 mL/vial

- Provided ready to use.
- Store upright and refrigerate at 2 to 10°C.
- Mix contents by gently inverting before use. Avoid bubble formation.
- Stable until the expiration date stated on the label when stored at 2 to 10°C.
- Vial is stable at 2 to 10°C for 90 days after initial use.
- Signs of possible deterioration are control values out of range.
- Refer to calibration card for exact concentrations.

S0:	Buffered bovine serum albumin (BSA), 0.1% sodium azide and 0.5% ProClin** 300.
S1, S2, S3, S4, S5:	CA 15-3 antigen at levels of approximately 10, 50, 100, 500 and 1000 U/mL in buffered BSA, 0.1% sodium azide and 0.5% ProClin 300.
Calibration Card:	1

Warnings and Precautions

- For *in vitro* diagnostic use.
- Patient samples and blood-derived products may be routinely processed with minimum risk using the procedure described. However, handle these products as potentially infectious according to universal precautions and good clinical laboratory practices, regardless of their origin, treatment, or prior certification. Use an appropriate disinfectant for decontamination. Store and dispose of these materials and their containers in accordance with local regulations and guidelines.
- Human source material used in the preparation of the reagent has been tested and found negative or non-reactive for Hepatitis B, Hepatitis C (HCV), and Human Immunodeficiency Virus (HIV-1 and HIV-2). Because no known test method can offer complete assurance that infectious agents are absent, handle reagents and patient samples as if capable of transmitting infectious disease.⁹
- Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. On disposal of liquids, flush with a large volume of water to prevent azide build-up.¹⁰
- Xi. Irritant: 0.5% ProClin 300.



R 43: May cause sensitization by skin contact.

S 28-37: After contact with skin, wash immediately with plenty of soap and water. Wear suitable gloves.

- The Material Safety Data Sheet (MSDS) is available upon request.

Procedure

Refer to the appropriate system manuals and/or Help system for information on calibration theory, configuring calibrators, calibrator test request entry, and reviewing calibration data.

Calibration Details

The Access BR Monitor Calibrators are provided at six levels – zero and approximately 10, 50, 100, 500 and 1000 U/mL. Assay calibration data are valid up to 56 days.

Calibrators run in duplicate.

Limitations of the Procedure

If there is evidence of microbial contamination or excessive turbidity in a reagent, discard the vial.

SAMPLE DILUENT A

REF 81908 (Vial)

REF A79783 (Diluent Pack)

Intended Use The Access Sample Diluent A is intended for use with Access assays to dilute patient samples containing analyte concentrations greater than the analyte specific S5 calibrator.

Summary and Explanation The analyte level in patient samples may exceed the level of the specific S5 calibrator. If a quantitative value is required, it will be necessary to dilute the samples in order to determine the analyte concentration.

Product Information Access Sample Diluent A
Cat. No. 81908: 4 mL/vial

- Provided ready to use.
- Allow the contents to stand for 10 minutes at room temperature.
- Mix gently by inverting before use. Avoid bubble formation.
- Stable until the expiration date stated on the vial label when stored at 2 to 10°C.

Diluent	Buffered BSA matrix with surfactant, < 0.1% sodium azide, 0.5% ProClin** 300.
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Cat. No. A79783: 2 diluent packs, 32.9 mL/pack

- Provided ready to use.
- Store upright and refrigerate at 2 to 10°C.
- Refrigerate at 2 to 10°C for a minimum of two hours before use on the instrument.
- Stable until the expiration date stated on the label when stored at 2 to 10°C.
- Stable at 2 to 10°C for 56 days after initial use of each well.
- Signs of possible deterioration are a broken elastomeric layer on the pack or control values out of range.
- If the diluent pack is damaged (i.e., broken elastomer), discard the pack.

R1a – R1e:	Buffered BSA matrix with surfactant, < 0.1% sodium azide, 0.5% ProClin 300.
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Warnings and Precautions

- For *in vitro* diagnostic use.
- Patient samples and blood-derived products may be routinely processed with minimum risk using the procedure described. However, handle these products as potentially infectious according to universal precautions and good clinical laboratory practices, regardless of their origin, treatment, or prior certification. Use an appropriate disinfectant for decontamination. Store and dispose of these materials and their containers in accordance with local regulations and guidelines.
- Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. On disposal of liquids, flush with a large volume of water to prevent azide build-up.¹⁰

- Xi. Irritant: 0.5% ProClin 300.



R 43: May cause sensitization by skin contact.

S 28-37: After contact with skin, wash immediately with plenty of soap and water. Wear suitable gloves.

- The Material Safety Data Sheet (MSDS) is available upon request.
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Procedure

Samples can be accurately measured within the analytic range of the lower limit of detection and the highest calibrator value of the specific assay. If a sample contains more analyte than the stated value of the S5 calibrator, dilute the sample following dilution instructions in the specific assay labeling under "Limitations of Procedure" in the reagent pack section. Refer to the appropriate system manuals and/or Help system for instructions on how to enter a sample dilution in a test request.

Limitations of the Procedure

If there is evidence of microbial contamination or excessive turbidity in the reagent, discard the vial.

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Printed in U.S.A.
Made in U.S.A.
Revised April 2010

