AIA-360 Assay Specifications
ST CA 19-9 Test Code 015

No.	Item	Data
1	Calib. Req	Show
2	Cal 1	0 U/mL
3	Cal 2	25 U/mL (example)
4	Cal 3	50 U/mL (example)
5	Cal 4	100 U/mL (example)
6	Cal 5	200 U/mL (example)
7	Cal 6	400 U/mL (example)
8	Cal Lot L	
9	Cal Lot R	
10	Unit	U/mL
11	Smpl. Vol	50
12	Dil. Vol	100
13	Assay L	1.0
14	Assay H	400 U/mL
15	Ref. L	
16	Ref. H	
17	Decimal	1
	Visible only in Test Mode	
18	Test Name	#19-9
19	Calib. No	6
20	Calib. Mul	3
21	Calib. Equ	4
22	Calib. CV	90
23	Assay Prtl	1
24	Factor1 A	1.000000
25	Factor1 B	0.000000
26	Factor2 A	1.000000
27	Factor2 B	0.000000
28	V. Conc	0.000000
29	G Origin	0.000000

AIA-900 Assay Specifications
ST CA 19-9 Test Code 015

No.	Item	Data
1	Code	15
2	ACT	1
3	Analyte	#CA199
4	Lot	***Enter current cal. lot no.
5	CAL 1	0 U/mL
6	CAL 2	25 U/mL (example)
7	CAL 3	50 U/mL (example)
8	CAL 4	100 U/mL (example)
9	CAL 5	200 U/mL (example)
10	CAL 6	400 U/mL (example)
11	Cal lot L	
12	Cal lot R	
13	Unit	U/mL
14	Decimal	1
15	Assay Low	1.0
16	Assay High	400
17	Reference Low	
18	Reference High	
19	Reschedule Low	1.0
20	Reschedule High	400
21	Factor A	1
22	Factor B	0
23	Sample Volume	50
24	Diluent Volume	100
25	2 Step reagent dispensing volume	0
26	Calibration code	7
27	CAL. No.	6
28	CAL. MUL.	3
29	CAL. EQU.	4
30	CAL. CV	90
31	DIL. SP1	1
32	DIL. SP2	1
33	DIL. CAL. (Calculation of dil ratio of conc.)	1
34	DIL. CNTL.	1
35	DIL. DO	10
36	DIL. AH.	5
37	DIL. CALC.	1
38	DIL. CODE	7
39	DIL. NAME	CA19-9
40	DIL. PRTY	3
41	PRE. SPVOL (Vol. of pretreated sample)	0
42	PRE. 1VOL (Vol. of pretreatment sol-1)	0
43	PRE. 2 VOL (Vol. of pretreatment sol-2)	0
44	PRE. CODE (pretreated sol. code)	0
45	PRE. NAME (pretreated sol. name)	0
46	Protocol	1
47	SYS. F_A	1
48	SYS. F_B	0
49	V. CONC.	0
50	G. ORIGIN	0

AIA-2000 Assay Specifications
ST CA 19-9 Test Code 015

No.	Item	Data
1	Unit	U/mL
2	Decimal places	1
3	Reference low	
4	Reference high	
5	Reschedule low	1.0
6	Reschedule high	400
7	Assay range low	1.0
8	Assay range high	400
9	Specimen diluent code	7
10	Specimen diluent name	CA19-9
11	Dilution factor for Sp. 1	1
12	Dilution factor for Sp. 2	1
13	Dilution factor for Control	1
14	Default multiplier for DO	100
15	Default multiplier for >H	10
16	Factor A	1.00000e+000
17	Factor B	0.00000e+000
18	Calibration code	4
19	Calibrator replicates	3
20	Calibrator lot	***Enter current cal. lot no.
21	Calibrator Concentration	
22	Cal - 01	0 U/mL
23	Cal - 02	25 U/mL (example)
24	Cal - 03	50 U/mL (example)
25	Cal - 04	100 U/mL (example)
26	Cal - 05	200 U/mL (example)
27	Cal - 06	400 U/mL (example)
28		
29		
30		
31		
32		
33		
34	Dilution factor for calibrator	1
35	Calibration period	90
36	Incubation time (10/40)	10
37	Assay protocol	1
38	Specimen volume	50
39	Diluent volume	100
40	Conjugate volume	0
41	Diluted conjugate volume	0
42	Pretreatment	0
43	Pretreatment specimen volume	0
44	Pretreatment Reagent code	0
45	Pretreatment Reagent name	0
46	Pretreatment Reagent 1 volume	0
47	Pretreatment Reagent 2 volume	0
48	System Factor	1
49	Calibration Code Check	007
50	Virtual Concentration	0.0
51	Graph Origin	0.0
52	Calculation with Dilution Factor	Yes

CA 19-9
ST AIA-PACK CA 19-9

Caution: The sale and distribution of this device is restricted by United States federal law to, by, or on the order of a physician. In addition, the use of this device is restricted to, by, or on the order of a physician. Because of differences in reagent specificity and assay methods, the concentration of CA 19-9 in a given specimen may vary with devices from different manufacturers. Values obtained with different assay methods cannot be used interchangeably. It is mandatory that results reported by the laboratory to the physician include the identity of the assay used. If the assay method for CA19-9 is changed during the course of monitoring patients with serial CA 19-9 levels, baseline values for the patients being serially monitored must be confirmed by additional sequential testing.

Name and Intended Use

ST AIA-PACK CA 19-9 is designed for IN VITRO DIAGNOSTIC USE ONLY for the quantitative measurement of CA 19-9 tumor associated antigen in human serum or heparinized plasma on Tosoh AIA Immunoassay analyzers. Serial testing using the ST AIA-PACK CA 19-9 assay is to be used as an aid in monitoring the disease status in patients who have been diagnosed with pancreatic cancer and who show measurable CA 19-9 results over the course of their disease. Results of CA 19-9 testing should be used in conjunction with other clinical methods that are standard of care for monitoring disease status in these patients.

Note: Patients must possess the ability to express the Lewis blood group antigen or they will be unable to produce the CA 19-9 antigen even in the presence of proven malignancy. A patient with a positive genotype for the Lewis antigen may produce varying levels of CA 19-9. Phenotyping for the presence of the Lewis blood group antigen may be insufficient to detect true Lewis antigen negative individuals.

Summary and Explanation of Test

According to the American Cancer Society, there will be an estimated 29,200 new cases of cancer of the pancreas in the United States (U.S.) in the year 2001, with 28,900 deaths.[1] The incidence rate for pancreatic cancer for men has been declining during the last decade but the rate among women has remained steady. Pancreatic cancer is the fourth leading cause of cancer deaths on an annual basis.

The overall survival of patients with cancer of the exocrine pancreas is nineteen percent (19%) during the first year after diagnosis but only three percent (3%) after five years. Since only ten percent (10%) of cancers of the pancreas appear to be contained completely within the pancreas at the time of diagnosis, surgical removal of the entire pancreatic tumor is successful in only a few patients. For patients who have surgery for apparently resectable cancer of the exocrine pancreas, the five-year survival rate is about twenty percent (20%), compared to three percent (3%) overall.

The clinical management of pancreatic cancer is extremely difficult. Most pancreatic cancers have in fact metastasized by the time of diagnosis. Management therefore consists of early diagnosis, and accurate staging of the disease using the TNM system of classification developed by the American Joint Commission on Cancer, as a guide to aggressive intervention or chemotherapy. These classifications can be grouped into the following stages of disease (Table 1).

Table 1

Disease Stage

Stage	T	N	M
0	Tis	0	0
I	1,2	0	0
II	3	0	0
III	1,2,3	1	0
IVA	4	Any	0
IVB	Any	Any	1

Treatment consists of surgical intervention, radiation therapy, chemotherapy and palliative care measures as well as nutritional management. Monitoring the progression of disease is critical in management of this disease; therefore, any effective adjunct to imaging and clinical assessment would be valuable in management of pancreatic cancer patients.

Pancreatic cancer is an intense target for new treatments since the disease has a very rapid course of progression and accounts for nearly 30,000 deaths in the U.S. each year. Previously published clinical studies typically have enrolled ten (10) or more patients that are well characterized by histological diagnosis of adenocarcinoma, by radiographically measurable disease, and by adequate bone marrow function as well as liver and kidney function.

The efficacy of treatment regimens has usually been measured by radiologic imaging techniques and clinical signs, the symptoms of pain, and, in many instances, the serum levels of CA19-92 tumor marker and correlated with patient survival. Typically, responses have been categorized as complete response, partial response, stable disease, or progressive disease.

The CA 19-9 antigen is a tumor–associated antigen synthesized by normal human pancreatic and biliary ductular cells. Despite the fact that normal pancreatic and bile secretions are rich in this antigen, very little of this marker appears in the blood of normal donors or in patients with benign disorders. On the other hand, most patients with adenocarcinoma of the pancreas have elevated levels of serum CA 19-9. Determinations of serum CA 19-9 concentrations have been used for monitoring or management of confirmed pancreatic cancer patients in evaluation of patient progress and treatment outcome. It should be emphasized that this test cannot be used in patients who are genotypically Lewis blood group antigen negative and do not produce CA 19-9 tumor associated antigen.

Principle of the Assay

The ST AIA-PACK CA 19-9 is a two-site immunoenzymometric assay performed entirely in the AIA-PACK. CA 19-9 present in the test sample is bound with monoclonal antibody (CAS243) immobilized on a magnetic solid phase and enzyme-labeled monoclonal antibody (CAS243) in the AIA-PACK. The magnetic beads are washed to remove unbound enzyme-labeled monoclonal antibody and are then incubated with a fluorogenic substrate, 4-methylumbelliferyl phosphate (4MUP). The amount of enzyme-labeled monoclonal antibody that binds to the beads is directly proportional to the CA 19-9 concentration in the test sample. A standard curve is constructed, and unknown sample concentrations are calculated using this curve.

Material Provided (ST AIA-PACK CA 19-9, Cat. No. 0025271)

5 trays x 20 test cups (ST AIA-PACK CA 19-9 Test Cup)

Plastic test cups containing lyophilized magnetic beads coated with mouse anti-CA 19-9 monoclonal antibody (CAS243) and mouse monoclonal antibody (CAS243) conjugated to bovine alkaline phosphatase with 0.1% sodium azide (lyophilized) as a preservative.

Materials Required But Not Provided

The following materials are not provided but are required to perform CA 19-9 analysis using the ST AIA-PACK (Cat. No. 0025271) on the AIA systems. They are available separately from Tosoh.

Materials	**Cat. No.**
AIA-SYSTEMS:	
AIA-360	0019945
AIA-900	0022930
AIA-900 9tray Sorter	0022931
AIA-900 19tray Sorter	0022932
AIA-2000 ST	0022100
AIA-2000 LA	0022101
AIA-PACK:	
AIA-PACK Substrate Set II	0020968
AIA-PACK Substrate/Reconstituent	
AIA-PACK CA 19-9 Calibrator Set	0020371
Calibrator #1 0 U/mL	
Calibrator #2 25 U/mL (approx.)	
Calibrator #3 50 U/mL (approx.)	
Calibrator #4 100 U/mL (approx.)	
Calibrator #5 200 U/mL (approx.)	
Calibrator #6 400 U/mL (approx.)	
AIA-PACK CA 19-9 Sample Diluting Solution	0020571
AIA-PACK Wash Concentrate Set	0020955
AIA-PACK Diluent Concentrate Set	0020956
AIA-PACK Detector Standardization Test Cups	0020970
AIA-PACK Sample Treatment Cups	0020971
Sample Cups	0018581
ADDITIONAL REQUIREMENTS: (Except AIA-360)	
Pipette Tips (1000/Pkg)	019215
Tip Rack (Empty)	019216
Preloaded Pipette Tips (96 Tips X 50 Racks)	996010
Preloaded Pipette Tips (96 Tips X 5 Racks)	996005

Only materials obtained from Tosoh should be used. Materials obtained elsewhere should not be substituted since assay performance is based strictly on Tosoh materials.

Warnings and Precautions

- The ST AIA-PACK CA 19-9 is intended for in vitro diagnostic use only.
- ℞ only. US Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner.
- Inspect the packaging and the exterior of the aluminum pouch or the vials for any sign of damage before use. If any damages are visible, contact your local Tosoh sales representative.
- Test cups from different lots should not be mixed within a tray.
- The ST AIA-PACK CA 19-9 contains sodium azide, which may react with lead or copper plumbing to form potentially explosive metal azides. When disposing of such reagents, always flush with large volumes of water to prevent azide build-up.
- Human sera is not used in the preparation of this product, however, since human specimens will be used for samples and other quality control products in the lab may be derived from human serum, please use standard laboratory safety procedures in handling all specimens and controls.
- For safe waste disposal, it is recommended that each laboratory complies with established laboratory procedures and local, state, and federal regulations.
- Do not use beyond the expiration date.
- The ST AIA-PACK CA 19-9 has been designed so that the high dose “hook effect” is not a problem for the vast majority of samples. Samples with CA 19-9 concentrations between 400 U/mL and 200,000 U/mL will read > 400 U/mL. The “hook effect” phenomenon may occur at CA 19-9 concentrations exceeding 200,000 U/mL.
- Serum, dust, metal, or microorganism contamination may cause degradation of reconstituted substrate solution. Store in a clean environment, away from direct sunlight and ultraviolet light.
- Tosoh Automated Immunoassays utilizing alkaline phosphatase-based technologies should not be used with samples from patients under Asfotase Alfa treatment.

Storage and Stability

All unopened materials are stable until the expiration date on the label when stored at the specified temperature.

Materials	Cat. No.
Refrigerator Temperature (2 - 8 C):	
ST AIA-PACK CA 19-9	0025271
AIA-PACK CA 19-9 Calibrator Set	0020371
AIA-PACK CA 19-9 Sample Diluting Solution	0020571
AIA-PACK Substrate Set II	0020968
AIA-PACK Wash Concentrate	0020955
AIA-PACK Diluent Concentrate	0020956

Room Temperature (18 - 25 °C):

Detector Standardization Test Cups	0020970
Sample Treatment Cups	0020971

AIA-PACK test cups may be stored for up to 24 hours at a room temperature of 18 - 25 °C. Calibrators must be kept tightly sealed and refrigerated at 2 - 8 °C. After opening, calibrators should be used within 7 days. After opening, Sample Diluting Solution is stable for up to 90 days refrigerated at 2 - 8 °C. Reconstituted substrate solution is stable for 3 days at 18 - 25 °C or 30 days at 2 - 8 °C. Working diluent and wash solutions are stable for 30 days at room temperature (18 - 25 °C). Reagents should not be used if they appear cloudy or discolored.

Specimen Collection and Handling

Serum or heparinized plasma is required for the assay. EDTA and citrated plasma SHOULD NOT BE USED.

No special patient preparation is necessary. When using serum, a venous blood sample is collected aseptically without additives. Store at 18 - 25 °C until a clot has formed (usually 15 - 45 minutes), then centrifuge to obtain the serum specimen for assay.

To use heparinized plasma, a venous blood sample is collected aseptically with the designated additive. Centrifuge and separate plasma from the packed cells as soon as possible.

Samples may be stored at 2 - 8 °C for up to 24 hours prior to analysis. If the analysis cannot be done within 24 hours, the sample should be stored frozen at -20 °C or below until analysis.

Repeated freeze-thaw cycles should be avoided. Turbid serum samples or samples containing particulate matter should be centrifuged prior to testing. Prior to assay, slowly bring frozen samples to room temperature (18 - 25 °C) and mix gently.

The sample required for analysis is 50 µL.

Procedure

1) Reagent Preparation

1a) Substrate Solution

Bring all reagents to room temperature (18 - 25 °C) before preparing the working reagent. Add the entire contents of the Substrate Reconstituent (100 mL) to the lyophilized Substrate and mix thoroughly to dissolve the solid material.

1b) Wash Solution

Add the entire contents of the Wash Concentrate (100 mL) to approximately 2.0 L of CAP Class I water or the clinical laboratory reagent water, mix well, and adjust the final volume to 2.5 L.

1c) Diluent

Add the entire contents of the Diluent Concentrate (100 mL) to approximately 4.0 L of CAP Class I water or the clinical laboratory reagent water, mix well, and adjust the final volume to 5.0 L.

2) Calibration

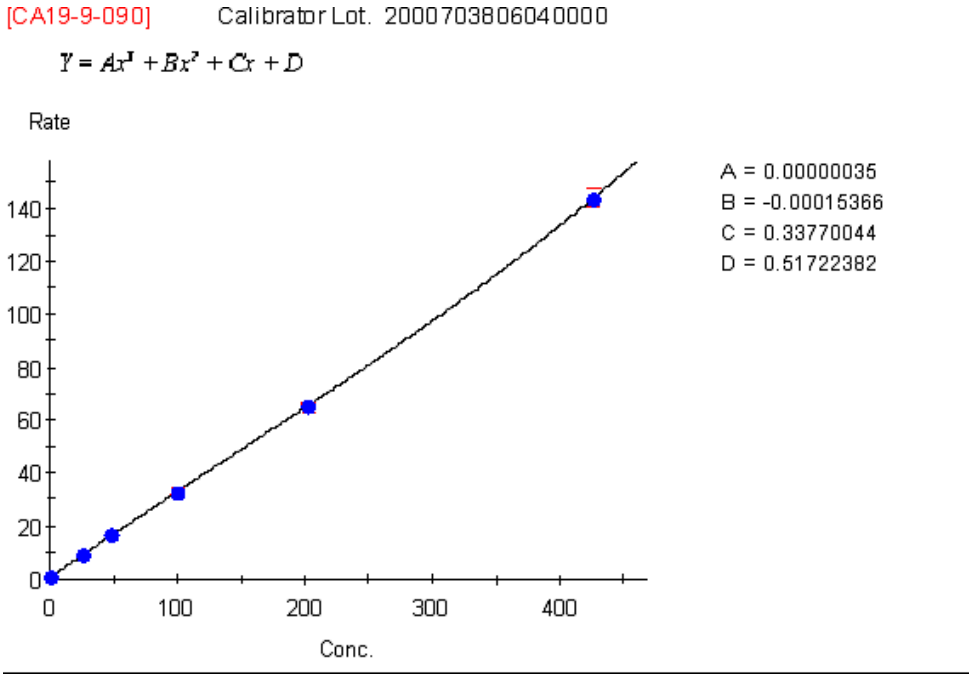
2a) Calibration Curve

The calibrators for use with the ST AIA-PACK CA 19-9 are prepared gravimetrically and are compared to internal reference standards.

The calibration curve for the ST AIA-PACK CA 19-9 is stable for up to 90 days. Calibration stability is monitored by quality control performance and is dependent on proper reagent handling and AIA System maintenance according to the manufacturer's instructions.

Recalibration may be necessary more frequently if controls are out of the established range for this assay or if certain service procedures are performed (e.g. temperature adjustment, sampling mechanism changes, or detector lamp adjustment or change). For further information regarding instrument operation, consult the AIA System Operator's Manual.

The sample calibration curve below shows the algorithm used to calculate the results. This is an example only. Actual results will vary depending on the Instrument type and lot number used.



2b) Calibration Procedure

Refer to the appropriate AIA System Operator's Manual for procedural instructions.

i) Verify that the calibrator lot and concentrations have been correctly entered into the software.

ii) The ST AIA-PACK CA 19-9 CALIBRATOR (1) is provided ready for use.

iii) Calibrator levels (2) - (6) for ST AIA-PACK CA 19-9 are lyophilized. Lyophilized calibrators should be reconstituted with 1.0 mL of CAP Class I water or the clinical laboratory reagent water. Tosoh recommends that all calibrators be run in triplicate.

2c) Calibration Acceptability criteria

i) The mean rate for the zero calibrator should be < 3.0 nM/sec.

ii) Since there is a direct relationship between concentration and rate, the rates should increase as the concentration increases.

iii) The replicate values should be within a 10% range.

2d) Calibration Review and Acceptance

i) Using the criteria above, review the calibration curve carefully.

ii) Edit the calibration if necessary, then accept the calibration.

iii) For further information regarding calibration, consult the specific AIA System Operator's Manual.

3) Quality Control

3a) Commercially Available Controls

Commercially available controls should be run at least once per day. It is recommended that at least two (2) levels of controls, normal and abnormal, be used. Laboratory policy for this particular assay designates the following:

Control Material: _____
Frequency: _____

Lot number of control material, acceptable limits, and corrective action to be taken if controls do not meet laboratory criteria will be found in a separate quality control document maintained by the laboratory.

3b) Quality Control Procedure

i) Assay quality control specimens as instructed in the specific Operator's Manual for your analyzer. In addition, refer to the AIA System Operator's Manual for detailed instructions on defining and editing the files.

ii) Quality control material to be run with this assay is defined by individual laboratory policy.

4) Specimen Processing

4a) Preparation

Following specific instructions in the Operator's Manual for the analyzer, place samples on the instrument appropriately.

4b) Assay Procedure

i) Ensure a sufficient quantity of ST AIA-PACK CA 19-9 test cups for the number of samples to be run.

ii) Load patient samples as instructed in the Operator's Manual and proceed with analysis. Note: The AIA-900 and AIA-2000 will require AIA-PACK Sample Treatment Cups if onboard dilutions are utilized.

Procedural Notes

1. Lyophilized Substrate must be completely dissolved.
2. Ligand assays performed by the Tosoh AIA System Analyzer require that the laboratory use water designated by the CAP Class I or by the clinical laboratory reagent water. Water should be tested at least once per month and should be free of particulate matter including bacteria. The pH of the water should also be routinely tested. For further information, consult the CLSI document GP40-A4-AMD, Preparation and Testing of Reagent Water in the Clinical Laboratory; Approved Guideline - Fourth Edition.
3. If a specimen CA 19-9 concentration is found to be greater than the linearity limit of the assay, 400 U/mL, the specimen should be diluted with the CA 19-9 Sample Diluting Solution and reassayed according to the Assay Procedure. The recommended dilution for samples containing greater than 400 U/mL is 1:10 or 1:100. It is desirable to dilute the sample so that the diluted sample reads between 25 and 400 U/mL. For further information on the dilution of specimens, refer to the AIA System Operator's Manual.
4. All AIA systems can store two different calibration curves for each analyte at one time. Therefore, up to two different lots of ST AIA-PACK CA 19-9 test cups can be used during the same run.
5. If the assay specifications for this test are not already in the system software, the specifications must be entered under test code 015.

Calculation of Results

AIA Systems read the rate of fluorescence produced by the reaction and automatically convert the rate to CA 19-9 concentration in U/mL.

For samples requiring dilution, the AIA-900 and AIA-2000 will automatically perform dilutions and calculate results if the dilution factors are entered into the software. Dilution factors may be entered into the Test File, or pre-defined dilution factors may be selected in Specimen Processing.

Evaluation of Results

Quality Control

In order to monitor and evaluate the precision of the analytical performance, it is recommended that commercially available control samples be assayed daily.

The minimum recommendations for the frequency of running internal control material are:

- After calibration, two levels of controls are run in order to accept the calibration curve.
- The two levels of controls are also repeated after calibration when certain service procedures are performed (e.g. temperature adjustment, sampling mechanism changes, maintenance of the wash probe or detector lamp adjustment or change).
- After daily maintenance, at least two levels of the control should be run in order to verify the overall performance of the Tosoh AIA System Analyzers.

If one or more control sample value(s) is out of the acceptable range, it will be necessary to investigate the validity of the calibration curve before reporting patient results.

Standard laboratory procedures should be followed in accordance with the regulatory agency under which the laboratory operates.

Limitations of the Procedure

ST AIA-PACK CA 19-9 SHOULD NOT BE USED AS A SCREENING TEST.

The results obtained from this assay should be used in conjunction with other data (e.g., symptoms, results of other tests, clinical impressions, therapy, etc.).

Using ST AIA-PACK CA 19-9, the highest concentration of CA 19-9 measurable without dilution is 400 U/mL, and the lowest measurable concentration is 1.0 U/mL (assay sensitivity).

Although the approximate value of the highest calibrator is approximately 400 U/mL, the exact concentration may be slightly different depending upon the lot. The assay specification, Assay Range High, should be defined as the upper limit of the assay range, 400 U/mL.

Although hemolysis has an insignificant effect on the assay, hemolyzed samples may indicate mistreatment of a specimen prior to assay and results should be interpreted with caution.

Lipemia has an insignificant effect on the assay except in the case of gross lipemia where spatial interference may occur.

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 falsely elevated values or occasionally falsely decreased values when tested for CA 19-9 using ST AIA-PACK CA 19-9.

A CA 19-9 result below the upper reference limit of normal does not indicate the absence of malignancy because patients with histopathologic evidence of pancreatic cancer may have CA 19-9 assay values within the range of normal individuals. Patients who do not secrete blood group Lewis antigen do not produce CA 19-9. Conversely, a CA 19-9 assay value exceeding the upper limit reference limit of normal does not necessarily indicate the presence of pancreatic malignancy since a small percentage of healthy individuals and individuals with non-malignant conditions as well as malignancy in other locations than the pancreas may have elevations in CA 19-9 assay results. A CA 19-9 assay value should not be interpreted as absolute evidence for the presence or absence of malignant disease of the pancreas.

Certain medications may interfere with assay performance. Specimens from patients taking medicines and/or medical treatment may show erroneous results. All results should be interpreted with respect to the clinical picture of the patient.

For a more complete understanding of the limitations of this procedure, please refer to the Specimen Collection and Handling, Warnings and Precautions, Storage and Stability, and Procedural Notes sections in this insert.

Expected Values

Each laboratory should determine a reference interval corresponding to the characteristics of the population being tested. As with all diagnostic procedures, clinical results must be interpreted with regard to concomitant medications administered to the patient.[3]

Clinical Performance Studies

Reference Limit for Apparently Healthy Individuals

Serum samples from 415 subjects who met the Red Cross criteria for giving blood and were considered to be free of apparent disease were analyzed for CA 19-9 using the ST AIA-PACK CA 19-9 assay. The cohort is comprised of 200 females (mean age = 58.3 years) and 215 men (mean age = 64.2 years).

Values for ST AIA-PACK CA 19-9 were determined in singlicate per manufacturer instructions. The mean values for the ST AIA-PACK assay were 20.6 U/mL for females (95% CI: 17.4, 23.7) and 22.8 U/mL for males (95% CI: 18.8, 26.8). Statistical analysis determined that differences in mean values between the sexes and for various age groups were not significant and values could be combined for normal subjects regardless of age or sex.

90% of all normal healthy subjects had a CA 19-9 value as measured by the ST AIA-PACK CA 19-9 assay below 47.0 U/mL (CI: 41.6, 50.3).

Benign Conditions

Three hundred and seventy-six subjects with benign conditions distributed into the four categories of chronic heart disease, pancreatic benign, GI/Colon benign and Urogenital benign were analyzed using the ST AIA-PACK CA 19-9. These cross-sectional samples were collected under IRB approval with signed informed consent documents obtained from each patient enrolled in the study. The table below shows the mean, median, standard error of the mean, and the 95% confidence limits for the four groups listed above. The order statistics for each condition was calculated and resampling techniques were used to estimate the 95% confidence intervals for the 5th, 90th and 95th order statistic. Analysis shows that the median values of these benign disease cohorts are of the same magnitude as the median value of the normal healthy subjects. All benign conditions except for those of the pancreas have distributions similar to the normal healthy cohort.

Sample Statistics by Benign Condition

ST AIA-PACK CA 19-9 Assay				
Statistic	**CHD**	**Pancreatic**	**GI/Colon**	**Urogenital**
N	96	87	96	97
Mean (U/mL)	17.1	28.2	21.0	21.8
Std. Error of Mean	1.4	2.8	2.0	1.8
Median (U/mL)	13.2	22.9	15.3	17.2
Minimum (U/mL)	0	0	0	0
Maximum (U/mL)	65.6	188	94.5	99.7
Skewness	1.3	3.1	1.7	1.9
Std. Error of Skewness	0.25	0.26	0.25	0.24
Kurtosis	1.6	16.3	3.4	4.7
Std. Error of Kurtosis	0.49	0.51	0.49	0.49

Treated Malignancy Cohorts

Samples from a total of 479 subjects treated for a variety of different cancers were analyzed using the ST AIA-PACK CA 19-9 assay. The sample statistics for each treated cancer group follows:

Sample Statistics By Cancer Cohort

Statistic	**Lung/ Liver**	**Breast/ Ovarian/ Cervical**	**Gallbladder**	**Pancreatic**	**Colo-rectal**	**Other**	
N	98	102	20	35	197	27	
Mean (U/mL)	176.0	55.9	693.3	3075.7	385.4	2138.8	
Std. Error of Mean	83.2	9.7	236.4	1407.7	116.7	1299.1	
Median (U/mL)	33.3	22.1	146.0	279.9	43.7	101.1	
Minimum (U/mL)	.0	.0	.0	.0	.0	.0	
Maximum (U/mL)	7980.0	542.5	3824.0	45750.0	17130.0	33770.0	
Skewness	9.0	3.6	1.9	4.4	8.0	4.3	
Std. Error of Skewness	.2	.2	.5	.4	.2	.4	
Kurtosis	85.5	13.8	3.2	21.5	72.2	20.1	
Std. Error of Kurtosis	.5	.5	1.0	.8	.3	.9	

For the ST AIA-PACK CA 19-9 assay, the upper limit of detection without dilution is 400 U/mL. In three of the cancer cohorts, the mean value for the cohort is greater than this limit. The table below demonstrates the percentage of patients in each cohort that had ST AIA-PACK CA 19-9 values above 400 U/mL. The range in parentheses represents an approximate 95% confidence interval based on the binomial distribution.

Percent of Treated Malignancy Patients with

CA19-9 values Exceeding 400 U/mL

Cohort	**% > 400 U/mL**
Lung/Liver	5.1 (2.3-11.5)
Breast/Ovarian/Cervical	3.0 (1.1-8.5)
Gallbladder	35.0 (19.1-59.2)
Pancreatic	40.0 (26.3-57.9)
Colorectal	10.1 (6.7-15.2)
Other	25.9 (13.8-46.3)

When 95% confidence intervals were constructed for the 5th, 50th (median) and 90th order statistic in each cohort, examination of these distributions indicates that CA 19-9 is elevated in treated gallbladder cancer, pancreatic cancer and the “other” cancer category. Examination of the cancers included in this “other” group reveals that they are similar in nature to gallbladder and pancreatic cancers (i.e. cancers of the bile ducts, duodenum, etc.) The distributions in the remaining treated cancer groups look similar to each other and are distinctly different from this first group.

Empirical Distribution (Order Statistics)
ST AIA-PACK CA 19-9 (U/mL)
By Treated Cancer Cohort

Percentile	Lung/ Liver	Breast/ Ovarian/ Cervical	Gallbladder	Pancreatic	Colorectal	Other
1	0.0	0.0	0.0	0.0	0.0	0.0
5 (95% CI)	**0.0 (0.0 to 5.5)**	**2.3 (0.0 to 5.3)**	**0.0 (0.0 to 17.9)**	**0.0 (0.0 to 16.8)**	**0.0**	**0.0 (0.0 to 28.8)**
10	1.8	5.3	3.2	8.6	0.0	3.0
15	11.8	6.1	11.0	15.8	5.7	22.7
20	13.7	10.5	16.8	24.8	7.7	29.0
25	16.4	12.0	21.0	43.6	11.0	30.8
30	20.0	13.4	26.3	69.4	17.9	32.2
35	23.7	16.7	32.4	76.8	22.1	32.7
40	26.7	17.2	40.8	107.3	26.8	37.2
45	28.9	19.0	96.6	134.3	33.1	56.2
50 (95% CI)	**33.3 (26.8 to 43.3)**	**22.1 (17.3 to 31.7)**	**146.0 (25.0 to 854.0)**	**279.9 (70.0 to 646.0)**	**43.7 (31.7 to 68.4)**	**101.1 (32.3 to 301.4)**
55	37.0	27.6	239.8	328.7	61.0	181.8
60	43.5	31.7	359.4	425.8	72.1	225.8
65	51.1	33.7	533.8	593.0	96.2	253.0
70	65.1	44.2	840.7	1,449.3	110.1	318.7
75	79.2	51.9	889.5	2,322.0	153.8	460.1
80	89.3	79.0	1,042.3	3,148.4	215.4	715.2
85	137.4	87.6	1,688.7	4,722.0	306.3	1,336.1
90 (95%CI)	**257.4 (123 to 395)**	**125.7 (85.0 to 180.0)**	**1,999.0 (827 to 3,624)**	**6,404.8 (2,776 to 19,780)**	**429.0 (311 to 977)**	**4,033.4 (445 to 19,332)**
95	396.4	188.3	2,748.6	11,595.6	1,395.4	9,384.8
99	1,698.8	526.2	3,608.9	36,920.2	6,337.4	27,600.2

Clinical Studies from Retrospective Serial Samples

A study was performed on prospectively collected specimens from several investigators in which CA 19-9 concentrations were measured three times (using the ST AIA-PACK CA 19-9 assay, the AIA-PACK CA 19-9 assay and an FDA cleared CA 19-9 RIA method) in serial serum specimens collected from 61 patients diagnosed with pancreatic cancer. Upon analysis of the CA 19-9 results, five patient series of the 61 showed results that were all indistinguishable from zero. It is presumed that these patients are Lewis non-secretors and that further analysis of the results from these 5 patient series would be inappropriate. Patient ID # 003, # 007, #014, #026 and #029 were removed from subsequent analyses. A total of 212 observations remained for 56 patients. The breakdown of the patient series is presented below. The average number of observations per patient is 3.79.

Patient Observation Series

Number in Series	Number of Observation Pairs	Frequency	Percent	Cumulative Percent
2	**1**	**19**	**33.9%**	**33.9%**
3	**2**	**13**	**23.2%**	**57.1%**
4	**3**	**9**	**16.1%**	**73.2%**
5	**4**	**7**	**12.5%**	**85.7%**
6	**5**	**3**	**5.4%**	**91.1%**
7	**6**	**1**	**1.8%**	**92.2%**
8	**7**	**1**	**1.8%**	**94.6%**
9	**8**	**2**	**3.6%**	**98.2%**
13	**12**	**1**	**1.8%**	**100.0%**

Disease

The table below presents the stage of the disease at the time of diagnosis for the 56 patients for whom we have evaluable serial samples. Only 8% of the patients had Stage I disease with 41% having advanced (Stage IV) malignancies.

Stage of Cancer at Time of Diagnosis

Stage at Diagnosis	Frequency	Percent (%)	Cumulative Percent (%)	
I	5	8.9	8.9	
II	19	33.9	42.8	
III	8	14.3	57.1	
IV	24	42.8	100.0	
Total	56	100.0		

The relationship between Stage at diagnosis and the presence of metastases is demonstrated in the table below. As would be logically expected, as the disease Stage progresses the percentage of patients with metastases increases.

Distribution of Metastases by Stage at Diagnosis

Known Metastases at time of Diagnosis:				
Stage	**Yes**	**No**	**Unknown**	**Total**
I	1	4	0	5
	20.0%	80.0%	0	100.0%
II	10	10	0	20
	50.0%	50.0%	0	100.0%
III	5	2	0	7
	71.4%	28.6%	0	100.0%
IV	19	3	2	24
	79.2%	12.5%	8.6%	100.0%
Total	35	19	2	56
	62.5%	33.9%	3.6%	100.0%

Time Interval under Study

The table below presents the time from diagnosis to first and to last collection date (in days) for each evaluable patient on whom serial samples were collected. In addition, the last column of the table shows the final clinical determination. Thirty-nine percent of the patients had a last clinical evaluation of progressive disease. The median time from diagnosis to first sample draw was 114 days (3.7 months). The median total time in the study was 322 days (10.6 months).

Time in Study

Subject ID	Time from Dx to First Draw (Days)	Total Time in Study (Days)	Last Clinical
001	232	757	Progressing
002	1507	1591	Progressing
004	0	181	Not Progressing
005	2113	3580	Not Progressing
006	1432	1851	Not Progressing
008	0	114	Not Progressing
009	0	182	Progressing
010	76	247	Not Progressing
011	1260	1541	Not Progressing
012	236	451	Not Progressing
013	80	133	Progressing
015	930	1832	Not Progressing
016	1282	2904	Not Progressing
017	1476	2226	Not Progressing
018	545	2558	Not Progressing
019	50	1006	Not Progressing
020	114	159	Not Progressing
021	428	581	Progressing
022	521	790	Not Progressing
023	1077	1427	Not Progressing
024	355	631	Progressing
025	1207	2407	Progressing
027	309	673	Not Progressing
028	340	1497	Progressing
030	23	250	Not Progressing
031	14	35	Progressing
032	663	761	Progressing
033	145	313	Not Progressing
034	6	61	Not Progressing
035	755	786	Progressing
036	0	54	Not Progressing
037	2052	2423	Progressing
038	8	59	Not Progressing
039	8	91	Progressing
040	25	83	Progressing

Subject ID	Time from Dx to First Draw (Days)	Total Time in Study (Days)	Last Clinical
041	16	779	Progressing
042	1001	1041	Progressing
043	1534	1589	Not Progressing
044	0	33	Not Progressing
045	384	489	Not Progressing
046	0	137	Progressing
047	52	238	Not Progressing
049	18	290	Not Progressing
050	28	119	Not Progressing
051	20	236	Not Progressing
052	104	315	Progressing
053	13	161	Progressing
054	7	89	Not Progressing
065	28	134	Progressing
066	42	115	Not Progressing
067	140	309	Progressing
068	40	57	Not Progressing
069	32	77	Not Progressing
070	265	322	Not Progressing
071	15	40	Progressing
072	61	138	Progressing

Association between CA 19-9 and Disease Status

Per visit analysis:

The following table shows the association between a significant positive change in a patient's CA 19-9 value as measured by the ST AIA-PACK CA 19-9 (significant change being defined as greater than 2.5 times the intra-assay CV% or 9.5%) and progression of the disease from one visit observation to the next. Results for the 156 evaluable observation pairs in this study are presented.

ST AIA-PACK Assay Results
Per Visit Analysis

	Clinical Status		
CA 19-9	**Progression**	**No Progression**	**Total**
Significant Marker Increase	30	39	69
No Significant Marker Increase	23	64	87
Total	53	103	156

Concordance Estimates
ST AIA-PACK CA 19-9

Statistic	Value	95% CI*	
		Lower Bound	Upper Bound
Concordance	0.602	0.513	0.692
Positive Concordance	0.566	0.434	0.698
Negative Concordance	0.621	0.553	0.689

*95% confidence intervals for each estimate of concordance are based on 10,000 permutations of the 2X2 Table with fixed marginal totals. For each permutation an estimate of Concordance, Positive Concordance and Negative Concordance was calculated. These estimates form approximate sampling distributions for each statistic.

Per patient analysis:

For the ST AIA-PACK CA 19-9, the following are statistical summaries of the 56 evaluable patient serial sets presented with the concordance estimates on a per patient basis with the 95% confidence intervals indicated.

Serial Patient Monitoring on a Per Patient Basis
ST AIA-PACK CA 19-9

	Disease Status		
Marker Change	**Progressive**	**Not Progressive**	**Total**
Increase>9.5%	22	18	40
No Significant Increase	7	9	16
Total	29	27	56

Serial Monitoring Examples

The following figures are examples of graphs generated on serials sample sets from two patients diagnosed with pancreatic cancer showing the changes in the CA 19-9 concentration over the clinical course of the disease as measured by ST AIA-PACK CA 19-9, AIA-PACK CA 19-9 and another manufacturer's FDA cleared CA 19-9 RIA method.

Figure A

Pancreatic Cancer Longitudinal Analysis

Patient ID	Sample ID	Sample Date	Disease Status	AIA CA19-9	ST AIA CA19-9	RIA CA19-9
PANS1-021	61422	01/03/95	PROGRESSING	1583.0	1541.5	2138
	61481	03/06/95	RESPONDING	249.6	259.8	569
	61541	04/17/95	RESPONDING	85.2	95.7	114
	61559	05/08/95	PROGRESSING	82.1	90.4	154
	61584	06/05/95	PROGRESSING	380.1	421.5	875

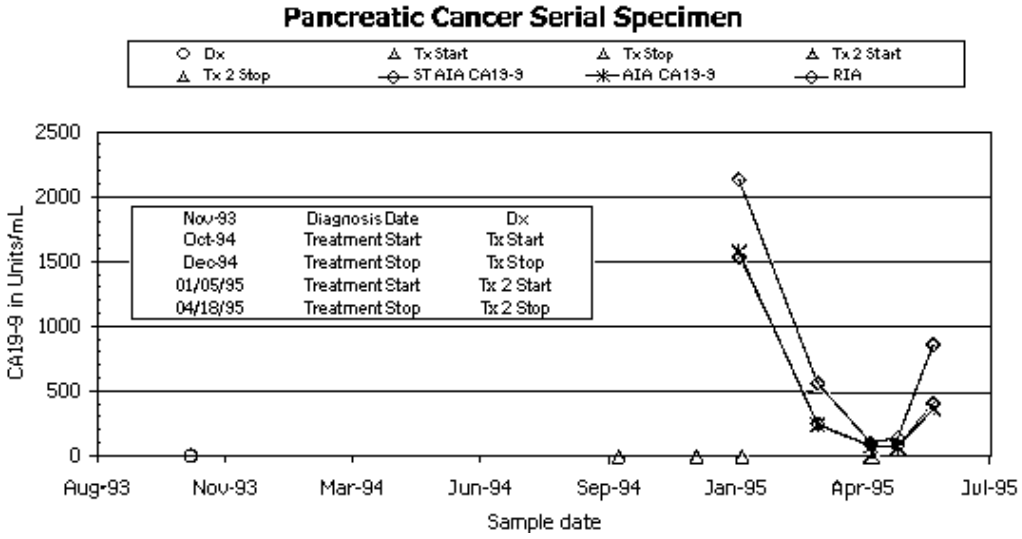
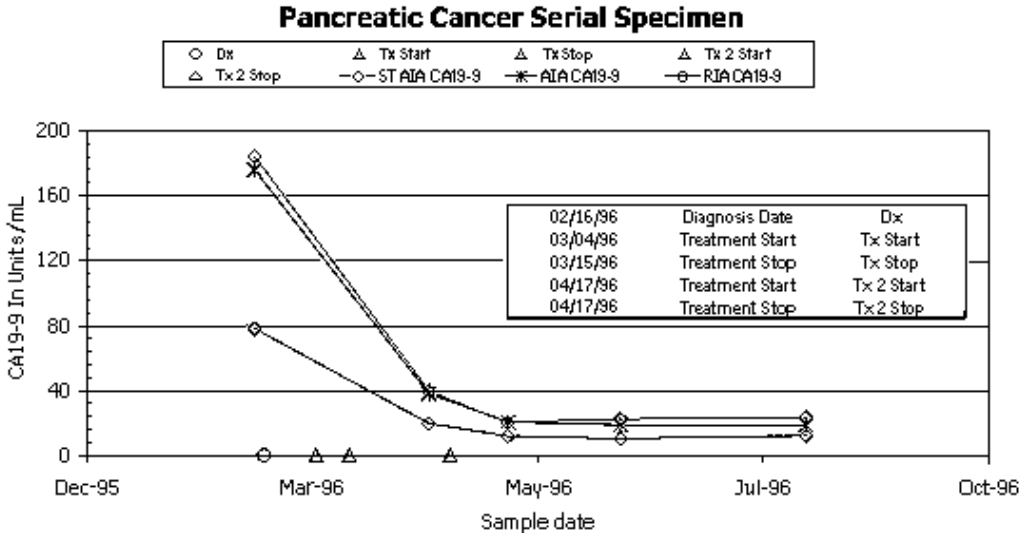


Figure B

Pancreatic Cancer Longitudinal Analysis

Patient ID	Sample ID	Sample Date	Disease Status	AIA CA19-9	ST AIA CA19-9	RIA CA19-9
PANS1-004	62043	02/13/96	PROGRESSING	176.2	184.5	78
	62244	04/10/96	RESPONDING	38.2	40.1	20
	62314	05/06/96	NED	20.8	20.2	12
	62396	06/12/96	NED	18.9	22.5	11
	62498	08/12/96	NED	19.0	23.9	12



Performance Characteristics

The following performance characteristics were determined using the Tosoh AIA Immunoassay Analyzers and the ST AIA-PACK CA 19-9 assay.

1) Accuracy

1a) Recovery:

Two serum pools were spiked with three different levels of CA 19-9 and assayed before and after spiking.

Sample	Initial Value (U/mL)	CA 19-9 Added (U/mL)	Expected Value (U/mL)	Measured Value (U/mL)	Percent Recovery (%)
Serum A1	7.92 7.92 7.92	9.53 19.06 38.11	17.45 26.98 46.03	17.36 27.72 45.48	99.5 102.7 98.8
Serum B1	10.36 10.36 10.36	9.53 19.06 38.11	19.89 29.42 48.47	19.44 29.84 47.27	97.7 101.4 97.5

1b) Dilution:

Three serum samples containing high concentrations of CA 19-9 were serially diluted with AIA-PACK CA 19-9 Sample Diluting Solution and assayed using ST AIA-PACK CA 19-9. Results obtained on these samples are presented below. Sample data was analyzed using EP Evaluator™ Release 4.0 for judgment of "clinical linearity" within the guidelines of 10% or less allowable system error.

Sample ID	Range (U/mL)	Observed Error (%)	Slope	Result
Sample L1	0.0 – 338.40	4.2	1.019	Linear
Sample L4	1.25 – 405.55	6.9	1.065	Linear
Sample L6	0.0 – 202.875	3.9	1.039	Linear

2) Precision

Per NCCLS (CLSI) guidelines and FDA guidance documents, imprecision was tested on the AIA-600 II using three serum pools of CA 19-9 with concentrations across the linear range of the assay run in quadruplicate in a randomized manner in two runs per day for ten days at two sites using two manufactured lots of ST AIA-PACK CA 19-9. An ANOVA table for a two-factor main effects model was generated for each panel-site-lot combination with the following results:

%CV for ST AIA-PACK CA19-9

By Site-Pool-Lot Combination

ST AIA-PACK™ CA 19-9 %CV						
Site 1						
	Pool 1		**Pool 2**		**Pool 3**	
Source	**Lot 17**	**Lot 19**	**Lot 17**	**Lot 19**	**Lot 17**	**Lot 19**
Day to Day	3.0	3.8	0.6	2.3	1.2	2.4
Run to Run	2.4	0.0	1.7	0.0	0.8	1.0
Within Run	4.5	5.5	4.5	5.0	3.8	4.7
Total	5.9	6.7	4.9	5.5	4.1	5.4
Site 2						
	Pool 1		**Pool 2**		**Pool 3**	
Source	**Lot 17**	**Lot 19**	**Lot 17**	**Lot 19**	**Lot 17**	**Lot 19**
Day to Day	0.6	1.5	1.1	2.6	0.3	2.8
Run to Run	0.0	0.0	0.3	0.9	0.8	0.0
Within Run	3.8	3.3	3.6	2.7	3.7	2.8
Total	3.8	3.6	3.8	3.9	3.8	4.0

Within run (Intra-assay) variation ranges from 2.7% to 5.5% across the site-pool-lot combinations.

Estimates for Run to Run variation across all site-pool-lot combinations never exceeded 2.4% with 11 out of the possible 12 estimates less than 2.0%.

Day-to-Day variation never exceeded 3.8% across all site-pool-lot combinations.

In second study, the run-to-run precision coefficient of variation was evaluated on the AIA NexIA using three control samples in a total of 20 runs. Within each run, one set of duplicates per control was assayed. The mean of each duplicate was used to obtain the pooled standard deviation (SD), which was then used to calculate the coefficient of variation (CV).

Run-to-Run Precision

Sample	Mean (U/mL)	Pooled SD (U/mL)	Coefficient of Variation (%)
Control A3	20.5	0.572	2.8
Control B3	30.3	0.766	2.5
Control C3	59.2	1.349	2.3

In a third study, the total precision on the AIA NexIA was determined by the duplicate assay of three controls in 20 separate runs. The means of each run were used to calculate the standard deviation (SD) and coefficient of variation (CV%).

Total Precision

Sample	Mean (U/mL)	Pooled SD (U/mL)	Coefficient of Variation (%)
Control A3	20.5	0.897	4.4
Control B3	30.3	1.202	4.0
Control C3	59.2	2.330	3.9

Sensitivity

The minimal detectable concentration (MDC) of ST AIA-PACK CA 19-9 is estimated to be 1.0 U/mL. The MDC is defined as that concentration of CA 19-9 corresponding to the rate of fluorescence that is two standard deviations from the mean rate of fluorescence of 20 replicate determinations of a zero calibrator.

Interference

Interference is defined, for purposes of this study, to be recovery outside of 10% of the known specimen mean concentration.

- Added hemoglobin (up to 390 mg/dL) does not interfere with the assay.
- Added free bilirubin (up to 17 mg/dL) and conjugated bilirubin (up to 19 mg/dL) do not interfere with the assay.
- Lipemia, as indicated by added triglyceride (up to 1660 mg/dL), does not interfere with the assay.
- Protein, as indicated by added albumin (concentrations up to 2.5 g/dL), does not interfere with the assay.
- Ascorbic acid (concentrations up to 20 mg/dL) does not interfere with the assay.
- EDTA (concentrations up to 10.0 mg/mL) does not interfere with the assay.
- Heparin (at concentrations of 500 U/mL) caused a slight positive interference with recovery at 118%.
- Tosoh Automated Immunoassays utilizing alkaline phosphatase-based technologies should not be used with samples from patients under Asfotase Alfa treatment.

The following pharmaceutical agents were tested at levels indicated and found not to cause analyte recovery outside 10%:

5'-fluorouracil (Adrucil),	1.0 mg/mL
Acetaminophen	0.2 mg/mL
Adriamycin (Doxorubicin HCl)	0.05 mg/dL
Tamoxifen	0.133 mg/mL
Coumarin	0.7 mg/mL
Cyclophosphamide(Cytoxan),	0.25 mg/mL
Paclitaxel,	3.5 x 10-6 mg/mL
Citrate, amethopterin hydrate (Methotrexate)	4.5 mg/mL
Mitoxanntrone (Novatrone),	0.5 mg/mL
Folinic acid (Leucovorin),	1.10 mg/mL
Mitomycin C	0.003 mg/mL
Aminoglutethimide	0.2 mg/mL
Cisplatin	0.025 mg/mL

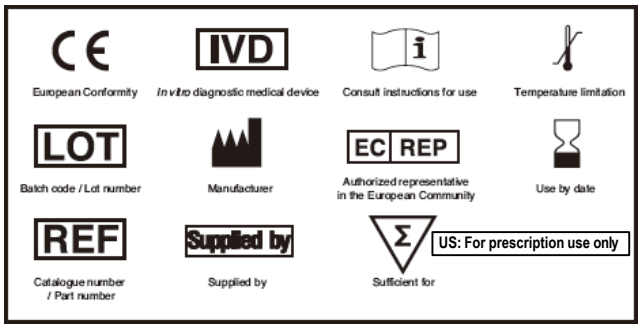
References

1. Greenlee, RT, Hill-Harmon, MB, Murray, T, and Thun, M. (2001) Cancer Statistics, 2001. CA Cancer J. Clin. 51:15-36.
2. Lillemoe, KD, Yeo, CY, and Cameron, JL. (2000) Pancreatic Cancer: State-of-the-Art Care. CA Cancer J. Clin. 50:241-268.
3. Young, D., Effects of Drugs on Clinical Laboratory Tests. 3rd Edition, American Association for Clinical Chemistry Press. 1990.

TOSOH CORPORATION
Bioscience Division
2-2-1 Yaesu, Chuo-ku, Tokyo 104-0028 Japan
Phone: +81 3 6636 3734
Fax: +81 3 6636 3627
Website: www.tosoh.com

Supplied by

TOSOH BIOSCIENCE, INC.
3600 Gantz Road,
Grove City, OH 43123 USA
Phone: +1 650 615 4970
Fax: +1 650 615 0415
Phone: (800) 248 6764
Fax: (800) 685 7595
Website: www.tosohbioscience.us



AIA-PACK
CA 19-9 Calibrator Set

Intended Use

The AIA-PACK CA 19-9 Calibrator Set is intended for IN VITRO diagnostic use only for the calibration of the ST AIA-PACK CA 19-9 Assays.

Summary and Explanation

The AIA-PACK CA 19-9 Calibrator Set contains bovine serum albumin with assigned levels of CA 19-9. Calibration should be performed according to the schedule indicated in the AIA System Operator's Manual. The calibrators in this set are prepared gravimetrically and compared to internal reference standards.

Material Provided (Cat. No. 0020371)

2 x 1 mL	Zero Calibrator		
	Bovine serum albumin containing no detectable concentration of CA 19-9 (0 U CA19-9/mL), and 0.1% sodium azide as preservative. (Ready for Use)		
2 x 1 mL	Calibrator No. 2	25	U/mL (approx.)
	Calibrator No. 3	50	U/mL (approx.)
	Calibrator No. 4	100	U/mL (approx.)
	Calibrator No. 5	200	U/mL (approx.)
	Calibrator No. 6	400	U/mL (approx.)
	Bovine serum albumin containing the assigned concentration of CA 19-9 (described on each vial), and 0.1% sodium azide as a preservative. (Lyophilized)		

Warnings and Precautions

- The AIA-PACK CA 19-9 Calibrator Set is for in vitro diagnostic use.
- These materials contain sodium azide, which may react with lead or copper plumbing to form potentially explosive metal azides. When disposing of such reagents, always flush with large volumes of water to prevent azide build-up.
- No human sera is used in the preparation of this product, but it is recommended that this product be handled with the same precautions as used for patient samples.
- Do not use beyond the expiration date.

Preparation and Storage

- Calibrator levels (2) - (6) for the AIA-PACK CA 19-9 assay are lyophilized. Add exactly 1.0 mL of CAP Class I water or the clinical laboratory reagent water to each bottle. Let stand a few minutes and then carefully swirl. Mix the calibrators gently but thoroughly prior to performing the calibration.
- Bring calibrator to room temperature (18 - 25 °C) for use.
- Always store the Calibrator Set in an upright position at 2 - 8 °C when not in use.

Stability

When stored unopened and refrigerated at 2 - 8 °C, the AIA-PACK CA 19-9 Calibrator Set is stable until the expiration date on the label. After opening, the calibrators should be used within 7 days.

Procedure

Refer to the CALIBRATION PROCEDURE in the AIA-PACK section of this document. For additional detailed procedural instructions regarding calibration, refer to the AIA System Operator's Manual.

Calibration Procedure

1. Verify that both the calibrator lot and concentrations have been correctly entered into the analyzer software.
2. Add the appropriate amounts of each calibrator to sample cups (refer to the instrument worklist for the amount required in each sample cup.)
3. Place the sample cups and the test cups on the analyzer as indicated on the worklist.
4. Tosoh recommends that all calibrators be run in triplicate.

Assignment of Values

The AIA-PACK CA 19-9 Calibrator Set contains assigned concentrations of CA 19-9. The assigned value is determined on a lot-to-lot basis and is designed to provide an assay calibration range of approximately 1.0 to 400.0 U/mL of CA 19-9. The calibrators in this set are prepared gravimetrically and compared to internal reference standards.

Results

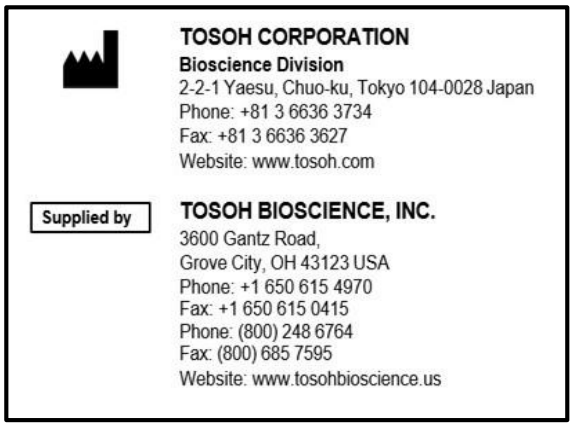
- The mean rate for the zero calibrator should be <3.0 nM/sec.
- Since there is a direct relationship between concentration and rate, the rates should increase as the concentration increases.
- The replicate values should be within a 10% range.

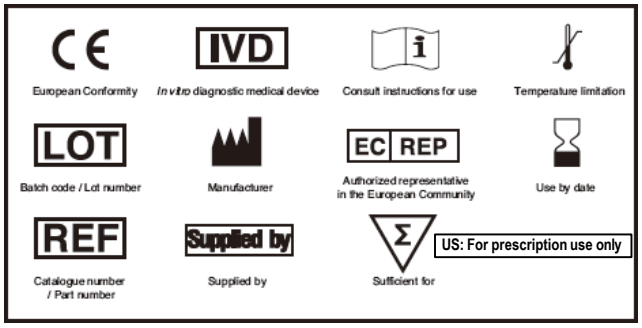
Limitations

The AIA-PACK CA 19-9 Calibrator Set is designed solely for use with AIA-PACK assay procedures.

References

1. AIA Analyte Application Manual (AAM). Tosoh Bioscience, Inc., Grove City, OH.
2. AIA-System Operator's Manual. Tosoh Bioscience, Inc., Grove City, OH.





AIA-PACK
CA 19-9 Sample Diluting Solution

Intended Use

The AIA-PACK CA 19-9 Sample Diluting Solution is intended for IN VITRO DIAGNOSTIC USE ONLY to dilute patient samples that have concentrations of CA 19-9 above the linear range of the assay.

Summary and Explanation

The AIA-PACK CA 19-9 Sample Diluting Solution contains bovine serum albumin with no detectable concentration of CA 19-9. This Sample Diluting Solution is to be used only with samples that are being tested for CA 19-9 concentrations using the ST AIA-PACK CA 19-9 assays.

Material Provided (Cat. No. 0020571)

4 x 4 mL	Sample Diluting Solution Bovine serum albumin containing no detectable concentration of CA 19-9 (0 U CA 19-9/mL), and 0.1% sodium azide as a preservative.

Warnings and Precautions

- The AIA-PACK CA 19-9 Sample Diluting Solution is for in vitro diagnostic use.
- These materials contain sodium azide, which may react with lead or copper plumbing to form potentially explosive metal azides. When disposing of such reagents, flush with large volumes of water to prevent azide build-up.
- Do not use beyond the expiration date.

Preparation and Storage

The AIA-PACK CA 19-9 Sample Diluting Solution is provided ready to use.

Always store the Sample Diluting Solution in an upright position at 2 - 8 °C when not in use.

Stability

When stored unopened and refrigerated at 2 - 8 °C, the AIA-PACK CA 19-9 Sample Diluting Solution is stable until the expiration date on the label. After opening, the Sample Diluting Solution is stable for up to 90 days when refrigerated at 2 - 8 °C.

Procedure

Refer to the AIA System Operator's Manual for additional procedural instructions regarding sample dilution. AIA-900 and AIA-2000 can be programmed to perform the dilution and the mathematical calculations automatically.

1. If a specimen is found to contain greater than the linearity limit of 400 U/mL, the specimen should be further diluted with the Sample Diluting Solution and assayed according to the instructions in the AIA System Operator's Manual.
2. The AIA 900 and AIA-2000 will perform dilutions automatically if the dilution factors are entered into the software prior to assaying the diluted sample.
3. The recommended dilution for specimen containing greater than the concentration of the highest calibrator is 1:10 or 1:100. However, it is desirable to dilute the serum samples that contain more than 400 U CA 19-9/mL so that the diluted sample reads between 25 and 400 U CA 19-9/mL.

Results

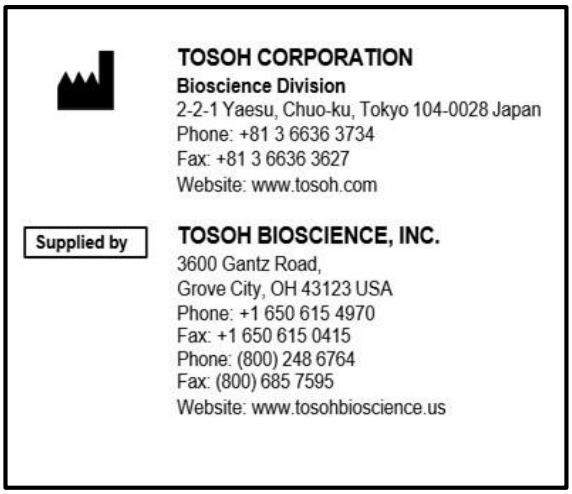
When an auto-dilution is performed, the AIA instrument will calculate the final result.

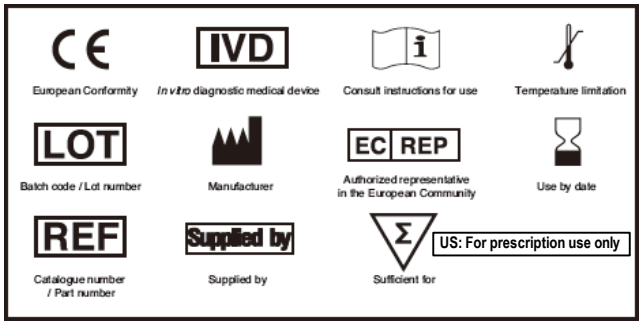
Limitations

The AIA-PACK CA 19-9 Sample Diluting Solution is designed solely for use with AIA-PACK assay procedures.

References

1. AIA Analyte Application Manual (AAM). Tosoh Bioscience, Inc., Grove City, OH.
2. AIA-System Operator's Manual. Tosoh Bioscience, Inc., Grove City, OH.


TOSOH CORPORATION
Bioscience Division
2-2-1 Yaesu, Chuo-ku, Tokyo 104-0028 Japan
Phone: +81 3 6636 3734
Fax: +81 3 6636 3627
Website: www.tosoh.com
Supplied by
TOSOH BIOSCIENCE, INC.
3600 Gantz Road,
Grove City, OH 43123 USA
Phone: +1 650 615 4970
Fax: +1 650 615 0415
Phone: (800) 248 6764
Fax: (800) 685 7595
Website: www.tosohbioscience.us


IVD
European Conformity
In vitro diagnostic medical device
Consult instructions for use
Temperature limitation
LOT
Batch code / Lot number
Manufacturer
EC REP
Authorized representative in the European Community
Use by date
REF
Catalogue number / Part number
Supplied by
Supplied by
Sufficient for
US: For prescription use only