ARCHITECT

SYSTEM

en

SCC

REF 8D18

F5-Y201-2/R2

SCC

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

REF	List Number	REAGENT LOT	Reagent Lot
IVD	*In Vitro* Diagnostic Medical Device	SN	Serial Number
LOT	Lot Number	REACTION VESSELS	Reaction Vessels
	Expiration Date	SAMPLE CUPS	Sample Cups
2°C 8°C	Store at 2-8˚C	SEPTUM	Septum
	Consult instructions for use	REPLACEMENT CAPS	Replacement Caps
	Manufacturer	ASSAY CD-ROM	Assay CD-ROM

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

Abbott

WARNING: The concentration of SCC 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 SCC 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 SCC levels serially is changed, additional sequential testing should be carried out. Prior to changing assays, the laboratory MUST confirm baseline values for patients being serially monitored.

WARNING: SCC reactive determinants are shed naturally in saliva and other body fluids. Contamination of the samples or the ARCHITECT disposables with saliva or aerosols (e.g., as a result of sneezing) may cause falsely elevated SCC assay values. It is recommended that all elevated values be reviewed and testing repeated as appropriate. Gloves should always be worn when handling samples, sample cups, reaction vessels, and septums. (Face masks are also recommended.)

NAME

ARCHITECT SCC (Squamous Cell Carcinoma)

INTENDED USE

The ARCHITECT SCC assay is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of squamous cell carcinoma antigen (SCC Ag) in human serum and plasma to be used as an aid in the management of patients with squamous cell carcinoma.

SUMMARY AND EXPLANATION OF TEST

SCC Ag is a subfraction of TA-4, a tumor antigen first described by Kato and Torigoe in 1977.[1] TA-4, obtained from squamous cell carcinoma tissue of the uterine cervix, has been characterized as a glycoprotein with a molecular weight of 48,000 daltons.[2] Isoelectric focusing and immunoblotting using anti-TA-4 rabbit serum reveals that TA-4 consists of at least 14 subfractions with pI's ranging from 5.44 to 6.62. SCC Ag, a purified subfraction, has a pI of 6.62.[3]

Early studies showed that TA-4 serum levels in women with cervical squamous cell carcinoma were frequently elevated above those found in healthy individuals.[1,2,4] Other studies have indicated serum TA-4 levels may reflect the extent of disease in women with cervical squamous cell carcinoma and that TA-4 levels could be useful as an adjunct in predicting prognosis, detecting recurrence and monitoring disease status.[4-8] In other types of squamous cell carcinoma (pharynx, larynx, palate, tongue and neck), detectable but low serum TA-4 levels have been reported.[2,4]

Crombach, *et al.*[9] measured SCC Ag in tissue extracts and sera of patients with nonmalignant and malignant gynecologic diseases. Cytosol SCC Ag concentrations were found to be significantly higher in normal squamous epithelia and in squamous cell carcinoma of the exocervix than those in normal columnar epithelia and in adenocarcinoma of the endocervix, endometrium, ovary and breast. In this study, the clinical sensitivity of SCC Ag serum levels for primary cervical cancer increased from 29% in stage I to 89% in stage IV.

SCC Ag has been studied in other squamous cell malignancies including lung, esophagus, head and neck, anal canal, and skin.[10-21] In general, a pattern similar to that seen with squamous cell carcinoma of the uterine cervix is seen with these cancers, i.e., the more advanced cancer stages are reportedly associated with higher SCC Ag levels. Researchers have reported that measurement of the antigen, in serial determinations, may indicate disease recurrence, residual disease following treatment, and response to therapy.[10-26]

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT SCC assay is a two-step immunoassay for the quantitative determination of SCC Ag in human serum and plasma, using CMIA technology with flexible assay protocols, referred to as Chemiflex.

In the first step, sample and anti-SCC Ag coated paramagnetic microparticles are combined. SCC Ag present in the sample binds to the anti-SCC Ag coated microparticles. After washing, anti-SCC Ag acridinium-labeled conjugate is added to create a reaction mixture in the second step. Following another wash cycle, pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of SCC Ag in the sample and the RLUs detected by the ARCHITECT *i* System optics.

For additional information on system and assay technology refer to the ARCHITECT System Operations Manual, Section 3.

REAGENTS

Reagent Kit, 100 Tests

ARCHITECT SCC Reagent Kit (8D18)

- **MICROPARTICLES** 1 Bottle (6.6 mL) Microparticles: Antibody to SCC Ag (mouse, monoclonal) coated microparticles in MES buffer with protein (bovine) stabilizer. Minimum concentration: 0.08% solids. Preservatives: Sodium Azide and other Antimicrobial Agents.
- **CONJUGATE** 1 Bottle (5.9 mL) Conjugate: Acridinium-labeled antibody to SCC Ag (mouse, monoclonal) conjugate in MES buffer with protein (bovine) stabilizer. Minimum concentration: 0.07 µg/mL. Preservatives: Sodium Azide and other Antimicrobial Agents.

Other Reagents

ARCHITECT *i* Pre-Trigger Solution

- **PRE-TRIGGER SOLUTION** Pre-Trigger Solution containing 1.32% (w/v) hydrogen peroxide.

ARCHITECT *i* Trigger Solution

- **TRIGGER SOLUTION** Trigger Solution containing 0.35N sodium hydroxide.

ARCHITECT *i* Wash Buffer

- **WASH BUFFER** Wash Buffer containing phosphate buffered saline solution. Preservative: Antimicrobial Agent.

WARNINGS AND PRECAUTIONS

- **IVD**
- For *In Vitro* Diagnostic Use
- Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Safety Precautions

- **CAUTION:** This product requires the handling of human specimens. It is recommended that all human sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens.[27] Biosafety Level 2[28] or other appropriate biosafety practices[29,30] 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.
- For product not classified as dangerous per European Directive 1999/45/EC as amended - Safety data sheet available for professional user on request.
- For a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Handling Precautions

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a kit or between reagent kits.**
- Before loading the ARCHITECT SCC Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that have settled during shipment. For microparticle mixing instructions, refer to the **PROCEDURE, Assay Procedure** section of this package insert.
- **Septums MUST be used to prevent reagent evaporation and contamination and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in this package insert.**
- To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.
  - Once a septum has been placed on an open reagent bottle, **do not invert the bottle** as this will result in reagent leakage and may compromise assay results.
  - Over time, residual liquids may dry on the septum surface. These are typically dried salts which have no effect on assay efficacy.
- For a detailed discussion of handling precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 7.

Storage Instructions

- The ARCHITECT SCC Reagent Kit must be stored at 2-8°C in an upright position and may be used immediately after removal from 2-8°C storage.
- When stored and handled as directed, reagents are stable until the expiration date.
- The ARCHITECT SCC Reagent Kit may be stored on board the ARCHITECT *i* System for a maximum of 30 days. After 30 days, the reagent kit must be discarded. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.
- Reagents may be stored on or off the ARCHITECT *i* System. If reagents are removed from the system, store them at 2-8°C (with septums and replacement caps) in an upright position. For reagents stored off the system, it is recommended that they be stored in their original trays and boxes to ensure they remain upright. **If the microparticle bottle does not remain upright (with a septum installed) while in refrigerated storage off the system, the reagent kit must be discarded.** For information on unloading reagents, refer to the ARCHITECT System Operations Manual, Section 5.

Indications of Reagent Deterioration

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 may require retesting. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

- The ARCHITECT SCC assay file must be installed on the ARCHITECT *i* System from the ARCHITECT *i* Assay CD-ROM (Addition C) prior to performing the assay. For detailed information on assay file installation and viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.
- For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.
- For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

The specimen collection tubes listed below were verified to be used with the ARCHITECT SCC assay. Other specimen collection tubes have not been tested with this assay.

- Human serum (including serum collected in serum separator tubes)
- Human plasma collected in:
  - Potassium EDTA
  - Sodium heparin
  - Sodium EDTA
- Liquid anticoagulants may have a dilution effect resulting in lower concentrations for individual patient specimens.
- The ARCHITECT *i* System does not provide the capability to verify specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the ARCHITECT SCC assay.

Specimen Conditions

- Do not use specimens with the following conditions:
  - heat-inactivated
  - grossly hemolyzed (> 500 mg/dL)
  - obvious microbial contamination
  - cadaver specimens or any other body fluids
- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter. Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- For optimal results, inspect all specimens for bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for serum and plasma collection tubes. Gravity separation is not sufficient for specimen preparation.
- Mix thawed specimens thoroughly by low speed vortexing or by inverting 10 times. Visually inspect the specimens. If layering or stratification is observed, continue mixing until specimens are visibly homogeneous.
- To ensure consistency in results, specimens must be transferred to a centrifuge tube and centrifuged at ≥ 10000 RCF (Relative Centrifugal Force) for 10 minutes before testing if
  - they contain fibrin, red blood cells, or other particulate matter,
  - they require repeat testing, or
  - they were frozen and thawed.

  Transfer clarified specimen to a sample cup or secondary tube for testing.
- Centrifuged specimens with a lipid layer on the top must be transferred to a sample cup or secondary tube. Care must be taken to transfer only the clarified specimen without the lipemic material.

Storage

- If testing will be delayed more than 24 hours, remove serum or plasma from the clot, red blood cells, or separator gel. Specimens may be stored for up to 7 days refrigerated at 2-8°C prior to being tested. If testing will be delayed more than 7 days, store frozen (-20°C or colder).
- Avoid multiple freeze/thaw cycles.

Shipping

- Before shipping specimens, it is recommended that specimens be removed from the clot, red blood cells, or separator gel.
- When shipping specimens, package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- Specimens may be shipped on wet or dry ice. Do not exceed the storage time limitations listed above.

PROCEDURE

Materials Provided

- 8D18 ARCHITECT SCC Reagent Kit

Materials Required but not Provided

- ARCHITECT *i* System
- ARCHITECT *i* **ASSAY CD-ROM** - WW (excluding US) - Addition C
- 8D18-02 ARCHITECT SCC Calibrators
- 8D18-11 ARCHITECT SCC Controls
- ARCHITECT *i* **PRE-TRIGGER SOLUTION**
- ARCHITECT *i* **TRIGGER SOLUTION**
- ARCHITECT *i* **WASH BUFFER**
- ARCHITECT *i* **REACTION VESSELS**
- ARCHITECT *i* **SAMPLE CUPS**
- ARCHITECT *i* **SEPTUM**
- ARCHITECT *i* **REPLACEMENT CAPS**
- Pipettes or pipette tips (optional)
- For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.

Assay Procedure

- Before loading the ARCHITECT SCC Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that have settled during shipment. After the first time the microparticles have been loaded, no further mixing is required.
  - **Invert the microparticle bottle 30 times.**
  - Visually inspect the bottle to ensure microparticles are resuspended. If microparticles remain adhered to the bottle, continue inverting the bottle until the microparticles have been completely resuspended.
  - **If the microparticles do not resuspend, DO NOT USE. Contact your local Abbott representative.**
  - Once the microparticles have been resuspended, place a septum on the bottle. For instructions on placing septums on bottles refer to the **Handling Precautions** section of this package insert.

- Load the ARCHITECT SCC Reagent Kit on the ARCHITECT *i* System.
  - Verify that all necessary assay reagents are present.
  - Ensure that septums are present on all reagent bottles.
- Order calibration, if necessary.
  - For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.
- Order tests.
  - For information on ordering patient specimens and controls and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- The minimum sample cup volume is calculated by the system and is printed on the Orderlist report. No more than 10 replicates may be sampled from the same sample cup. To minimize the effects of evaporation, verify adequate sample cup volume is present before running the test.
  - Priority: 150 µL for the first ARCHITECT SCC test plus 25 µL for each additional ARCHITECT SCC test from the same sample cup.
  - ≤ 3 hours on board: 150 µL for the first ARCHITECT SCC test plus 25 µL for each additional ARCHITECT SCC test from the same sample cup.
  - > 3 hours on board: additional sample volume is required. For information on sample evaporation and volumes, refer to the ARCHITECT System Operations Manual, Section 5.
  - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare calibrators and controls.
  - Mix ARCHITECT SCC Calibrators and Controls by gentle inversion before use.
  - To obtain the recommended volume requirements for the ARCHITECT SCC Calibrators and Controls, hold the bottles **vertically** and dispense 4 drops of each calibrator or 4 drops of each control into each respective sample cup.
- Load samples.
  - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
- Press RUN.
- For additional information on principles of operation, refer to the ARCHITECT System Operations Manual, Section 3.
- For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.

Specimen Dilution Procedures

- Specimens with an SCC value exceeding 70 ng/mL are flagged with the code ">70" and may be diluted using the Manual Dilution Procedure.
- ARCHITECT SCC assay cannot use the Automated Dilution Protocol.
- Manual dilutions should be performed as follows:
  - The suggested dilution for the ARCHITECT SCC assay is 1:10.
  - For a 1:10 dilution, add 20 µL of the patient specimen to 180 µL of ARCHITECT SCC Calibrator A (8D18-02).
  - To avoid contamination of Calibrator A, dispense several drops of Calibrator A into a clean test tube prior to pipetting.
  - The operator must enter the dilution factor in the Patient or Control order screen. The system will use this dilution factor to automatically calculate the concentration of the sample before dilution and report the result. The dilution should be performed so that the diluted result reads greater than 1.0 ng/mL.
- For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

Calibration

- To perform an ARCHITECT SCC calibration, test Calibrators A, B, C, D, E and F in duplicate. A single sample of all levels of SCC controls must be tested to evaluate the assay calibration. Ensure that assay control values are within the concentration ranges specified in the control package insert. Calibrators should be priority loaded.
- Calibration Range: 0 - 70 ng/mL.
- Once an ARCHITECT SCC calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:
  - A reagent kit with a new lot number is used.
  - Controls are out of range.
- For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

QUALITY CONTROL PROCEDURES

The recommended control requirement for the ARCHITECT SCC assay is that a single sample of each control be tested once every 24 hours each day of use. If your laboratory quality control procedures require more frequent use of controls to verify test results, follow those procedures. Additional controls may be tested in conformance with local, state, and/or federal regulations or accreditation requirements and your laboratory's quality control policy.

Each laboratory should establish control ranges to monitor the acceptable performance of the assay. If a control is out of its specified range, the associated test results are invalid and samples must be retested. Recalibration may be indicated.

Verification of Assay Claims

For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B.

RESULTS

The ARCHITECT SCC assay utilizes a 4 Parameter Logistic Curve fit data reduction method (4PLC, Y weighted) to generate a 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 ARCHITECT System Operations Manual, Section 5.

Measurement Range (Reportable Range)

- The measurement range of the ARCHITECT SCC assay is 0.1 ng/mL to 70 ng/mL.

LIMITATIONS OF THE PROCEDURE

- If the SCC Ag results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- For diagnostic purposes, results should be used in conjunction with other data; e.g., symptoms, results of other tests, clinical impressions, etc.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.[31] Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous values may be observed. Additional information may be required for diagnosis.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA).[32,33] Specimens containing HAMA may produce anomalous values when tested with assay kits (such as ARCHITECT SCC) that employ mouse monoclonal antibodies.[32]
- The ARCHITECT SCC assay should not be used as a cancer screening test.
- The concentration of SCC Ag in a given specimen, determined with assays from different manufacturers, can vary due to differences in assay methods, calibration, and reagent specificity.

EXPECTED VALUES

95.6% of the healthy subjects (n=616) had SCC values of 1.5 ng/mL or less at two laboratories.

It is recommended that each laboratory establish its own expected reference range for the population of interest.

SCC Ag blood levels, regardless of value, should not be interpreted as absolute evidence for the presence or absence of malignant disease. In patients with suspected or known cancer, other tests and procedures must also be considered for diagnosis and good management.

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

Precision was determined as described in the National Committee for Clinical Laboratory Standards (NCCLS) Protocol EP5-A.[34] Six samples consisting of three serum based panels and three SCC Controls were assayed in replicates of two at two separate times per day for twenty days (n=80 for each sample), using three lots of reagents and calibrations performed at each testing. Data from this study are summarized in the following table.

Reproducibility of ARCHITECT SCC

			Within Run		Total	
Sample	Lot	Mean SCC (ng/mL)	SD	% CV	SD	% CV
Low Control	1	1.97	0.085	4.3	0.100	5.1
	2	1.98	0.065	3.3	0.079	4.0
	3	1.92	0.089	4.6	0.108	5.6
Medium Control	1	9.90	0.379	3.8	0.496	5.0
	2	9.91	0.456	4.6	0.453	4.6
	3	9.81	0.482	4.9	0.463	4.7
High Control	1	49.23	2.332	4.7	2.587	5.3
	2	49.55	2.106	4.3	2.160	4.4
	3	49.45	1.917	3.9	2.203	4.5
Panel 1	1	1.49	0.075	5.0	0.088	5.9
	2	1.52	0.075	5.0	0.082	5.4
	3	1.42	0.072	5.1	0.080	5.6
Panel 2	1	7.37	0.275	3.7	0.353	4.8
	2	7.65	0.308	4.0	0.398	5.2
	3	7.13	0.281	3.9	0.333	4.7
Panel 3	1	53.55	2.031	3.8	2.338	4.4
	2	55.03	2.115	3.8	2.421	4.4
	3	52.28	1.980	3.8	2.065	4.0

Recovery

Known amounts of SCC were added to normal human serum and plasma samples. The concentration of SCC was determined using the ARCHITECT SCC assay and the resulting percent recovery was calculated.

Recovery

Sample Type	Endogenous Level (ng/mL)	SCC Added (ng/mL)	SCC Observed (ng/mL)	Percent Recovery
Serum				
1	0.38	10.09	10.35	98.8
	0.38	52.53	49.53	93.6
2	0.35	10.09	10.67	102.3
	0.35	52.53	52.48	99.2
3	0.37	10.09	10.90	104.4
	0.37	52.53	51.10	96.6
4	0.25	10.09	10.14	98.0
	0.25	52.53	48.29	91.5
5	0.31	10.09	10.48	100.8
	0.31	52.53	51.65	97.7
Plasma				
1	0.49	10.05	10.50	99.6
	0.49	50.82	50.66	98.7
2	0.44	10.05	9.88	93.9
	0.44	50.82	46.85	91.3
3	0.41	10.05	10.11	96.5
	0.41	50.82	49.17	95.9
4	0.49	10.05	10.45	99.1
	0.49	50.82	50.64	98.7
5	0.48	10.05	10.00	94.7
	0.48	50.82	49.65	96.8

$$\% \text{ Recovery} = \frac{\text{SCC Observed (ng/mL)} - \text{Endogenous Level (ng/mL)}}{\text{SCC Added (ng/mL)}} \times 100$$

Analytical Sensitivity

The sensitivity of the ARCHITECT SCC assay was calculated to be better than 0.1 ng/mL. Sensitivity is defined as the concentration at two standard deviations above the mean RLU for the ARCHITECT SCC Calibrator A (0 ng/mL) and represents the lowest measurable concentration of SCC that can be distinguished from zero.

Specificity

The specificity of the ARCHITECT SCC assay was determined by testing sera containing the compounds listed below. These compounds showed less than 10% interference in the ARCHITECT SCC assay at the levels indicated.

Test Compound	Test Concentration
Bilirubin	20 mg/dL
Hemoglobin	500 mg/dL
Total Protein	12 g/dL
Triglycerides	3000 mg/dL

Carryover

No detectable carryover (less than 0.05 ng/mL) was observed when a sample containing 150 ng/mL of SCC was assayed.

BIBLIOGRAPHY

1. Kato H, Torigoe T. Radioimmunoassay for Tumor Antigen of Human Cervical Squamous Cell Carcinoma. *Cancer* 1977;40:1621-8.
2. Kato H, Morioka H, Aramaki S, and Torigoe T. Radioimmunoassay for Tumor-Antigen of Human Cervical Squamous Cell Carcinoma. *Cell Mol Biol* 1979;25:51-6.
3. Ikeda I. Two-Site Radioimmunometric (Sandwich) Assay of SCC Antigen Using Monoclonal Antibodies. In: Kato H, de Bruijn HWA, Ebert W, Herberman R, Johnson J, editors. SCC Antigen in the Management of Squamous Cell Carcinoma. Princeton: Excerpta Medica. 1987:215-26.
4. Kato H, Miyauchi F, Morioka H, Fujino T, and Torigoe T. Tumor Antigen of Human Cervical Squamous Cell Carcinoma. *Cancer* 1979;43: 585-90.
5. Kato H, Morioka H, Tsutsui H, Aramaki S, and Torigoe T. Value of Tumor-Antigen (TA-4) of Squamous Cell Carcinoma in Predicting the Extent of Cervical Cancer. *Cancer* 1982;50:1294-6.
6. Kato H, Morioka H, Aramaki S, Tamai K, and Torigoe T. Prognostic Significance of the Tumor Antigen TA-4 in Squamous Cell Carcinoma of the Uterine Cervix. *Am J Obstet Gynecol* 1983;145:350-4.
7. Kato H, Tamai K, Morioka H, Nagai M Nagaya T, and Torigoe T. Tumor-Antigen TA-4 in the Detection of Recurrence in Cervical Squamous Cell Carcinoma. *Cancer* 1984;54:1544-6.

8. Maruo T, Shibata K, Kimura A, Hoshina M, and Mochizuki M. Tumor Associated Antigen TA-4 in the Monitoring of the Effects of Therapy for Squamous Cell Carcinoma of the Uterine Cervix. *Cancer* 1985;56:302-8.
9. Crombach G, Scharl A, Vierbuchen M, Wurz H, and Bolte A. Detection of Squamous Cell Carcinoma Antigen in Normal Squamous Epithelia and in Squamous Cell Carcinoma of the Uterine Cervix. *Cancer* 1989;63:1337-42.
10. Yagi H, Danno K, Maruguchi Y, Yamamoto M, and Imamura I. Significance of Squamous Cell Carcinoma (SCC) -Related Antigens in Cutaneous SCC. *Arch Dermatol* 1987;123:902-6.
11. Yoshimura Y, Harada T, Oka M, Sugihara T, and Kishimoto H. Squamous Cell Carcinoma Antigen in the Serum of Oromaxillary Cancer. *Int J Oral Maxillofac Surg* 1988;17:49-53.
12. Petrelli N, Shaw N, Bhargava A, Daufeldt J, Herrera L, Stule J, *et al.* Squamous Cell Carcinoma Antigen as a Marker for Squamous Cell Carcinoma of the Anal Canal. *J Clin Oncol* 1988;6:782-5.
13. Yamanaka N, Himi T, Harabuchi Y, Hoki K, and Kataura A. Soluble Immune Complexes and Squamous Cell Carcinoma-Related Antigens in Patients with Head and Neck Cancer. *Cancer* 1988;62:1932-8.
14. Mino N, Iio A, and Hamamoto K. Availability of Tumor-Antigen 4 as a Marker of Squamous Cell Carcinoma of the Lung and Other Organs. *Cancer* 1988;62:730-4.
15. Eibling D, Johnson J, and Wagner R. Radioimmunoassay for SCC Antigen in the Diagnosis of Squamous Cell Carcinoma of the Head & Neck. *Laryngoscope* 1989;99:117-24.
16. Johnson J, Wagner R, Eibling D, and Su S. Radioimmunoassay for SCC Antigen in the Diagnosis of Squamous Cell Carcinoma of the Head & Neck: A Preliminary Report. In: Kato H, de Bruijn HWA Ebert W, Herberman R, Johnson J. editors. SCC Antigen in the Management of Squamous Cell Carcinoma. Princeton: Excerpta Medica. 1987:112-23.
17. Savary L, Tuchais E, Oury M, Daver A, Tuchais C, and Larra F. Serial Radioimmunoassay of SCC Antigen for Diagnosis and Monitoring of Bronchial Squamous Cell Carcinoma: Preliminary Results. In: Kato H, de Bruijn HWA Ebert W, Herberman R, Johnson J. editors. SCC Antigen in the Management of Squamous Cell Carcinoma. Princeton: Excerpta Medica. 1987:193-201.
18. Fischback W. SCC Antigen, CEA and NSE in Squamous Cell Carcinoma and Other Types of Lung Cancer. In: Kato H, de Bruijn HWA Ebert W, Herberman R, Johnson J. editors. SCC Antigen in the Management of Squamous Cell Carcinoma. Princeton: Excerpta Medica. 1987:186-92.
19. Bonfrer J, Zandwijk N, and Higers F. SCC Antigen Levels in Patients with Squamous Cell Carcinoma of the Lung. In: Kato H, de Bruijn HWA Ebert W, Herberman R, Johnson J. editors. SCC Antigen in the Management of Squamous Cell Carcinoma. Princeton: Excerpta Medica. 1987:171-4.
20. Burtin P, Bonali A, Boyer J, Daver A, Larra F, and Ronceray J. Diagnostic and Prognostic Value of Serum Levels of SCC Antigen in Patients with Esophageal Epidermoid Carcinomas: A Retrospective Study of 64 Patients. In: Kato H, de Bruijn HWA Ebert W, Herberman R, Johnson J. editors. SCC Antigen in the Management of Squamous Cell Carcinoma. Princeton: Excerpta Medica. 1987:142-8.
21. Damle SR. Usefulness of Squamous Cell Carcinoma Antigen (SCC) in Carcinoma of Esophagus. *Clin Chem* 1988;34(6):1299-1300.
22. Senekjian EK, Young JM, Weiser P, *et al.* SCC Antigen in Patients with Malignant and Other Gynecological Disease (Summary). In: Kato H, de Bruijn HWA Ebert W, Herberman R, Johnson J. editors. SCC Antigen in the Management of Squamous Cell Carcinoma. Princeton: Excerpta Medica. 1987:75-7.
23. Henry RJ, Dodd JK, Tyler JP, and Houghton CR. SCC Tumor Marker and Its Relationship to Clinical Stage in Squamous Cervical Cancer. *Aust NZl Obstet Gynaecol* 1987;27(4):338-40.
24. de Bruijn HWA, Duk MJ, Feuren GJ. Kravis M, ten Hoor KA, and Aalders JG. The Tumor Markers CA 125 and SCC in Gynaecological Oncology. *Scand J Clin Lab Invest* 48 Suppl. 1988;190:36-9.
25. Kenter G, Bonfrer JMG, and Heintz APM. Pretreatment Tumor-Antigen TA-4 in Serum of Patients With Squamous Cell Carcinoma of the Uterine Cervix. *Br J Cancer* 1987;56:157-8.
26. Fuith LC, Daxenbichler G. Squamous Cell Carcinoma Antigen in Patients with Cancer of the Uterine Cervix. *Gynecol Obstet Invest* 1988;26:77-82.
27. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne pathogens.
28. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories.* 5th ed. Washington, DC: US Government Printing Office, January 2007.
29. World Health Organization. *Laboratory Biosafety Manual.* 3rd ed. Geneva: World Health Organization; 2004.
30. Clinical and Laboratory Standards Institute. *Protection of Laboratory Workers from Occupationally Acquired Infections: Approved Guideline - Third Edition.* CLSI Document M29-A3. Wayne, PA: Clinical and Laboratory Standards Institute, 2005.
31. Boscato LM, Stuart MC. Heterophilic Antibodies: A Problem for All Immunoassays. *Clin Chem* 1988;34:27-33.
32. Primus FJ, Kelley EA, Hansen HJ, *et al.* "Sandwich"-Type Immunoassay of Carcinoembryonic Antigen in Patients Receiving Murine Monoclonal Antibodies for Diagnosis and Therapy. *Clin Chem* 1988;34:261-4.
33. Schroff RW, Foon KA, Beatty SM, *et al.* Human Anti-Murine Immunoglobulin Responses in Patients Receiving Monoclonal Antibody Therapy. *Cancer Res* 1985;45:879-85.
34. National Committee for Clinical Laboratory Standards. *Evaluation of Precision Performance of Clinical Chemistry Devices*; Approved Guideline. NCCLS Document EP5-A (ISBN 1-56238-368-X). NCCLS, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898, USA, 1999.

ABBOTT
Max-Planck-Ring 2
65205 Wiesbaden
Germany
+49-6122-580

Produced by
DENKA SEIKEN CO., LTD.
Tokyo, Japan for
ABBOTT Diagnostics Division

November 2009