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

Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Key to symbols used

<table>
<thead>
<tr>
<th>REF</th>
<th>List Number</th>
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<tr>
<td>IVD</td>
<td>In Vitro Diagnostic Medical Device</td>
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<td></td>
<td>Expiration Date</td>
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<tr>
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<td>Store at 2-8°C</td>
</tr>
<tr>
<td></td>
<td>Consult instructions for use</td>
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<td>Manufacturer</td>
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<table>
<thead>
<tr>
<th>REAGENT LOT</th>
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<tr>
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<tr>
<td>REACTION VESSELS</td>
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<tr>
<td>SAMPLE CUPS</td>
<td>Sample Cups</td>
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<tr>
<td>SEPTUM</td>
<td>Septum</td>
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<td>REPLACEMENT CAPS</td>
<td>Replacement Caps</td>
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<tr>
<td>ASSAY CD-ROM</td>
<td>Assay CD-ROM</td>
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</table>

See REAGENTS section for a full explanation of symbols used in reagent component naming.
response to therapy. 10-26
are reportedly associated with higher SCC Ag levels. Researchers have
cervix is seen with these cancers, i.e., the more advanced cancer stages
pattern similar to that seen with squamous cell carcinoma of the uterine
lung, esophagus, head and neck, anal canal, and skin. 10-21 In general, a
SCC Ag has been studied in other squamous cell malignancies including
Ag serum levels for primary cervical cancer increased from 29% in stage I
endometrium, ovary and breast. In this study, the clinical sensitivity of SCC
with nonmalignant and malignant gynecologic diseases. Cytosol SCC Ag
purified subfraction, has a pI of 6.62. 3
of at least 14 subfractions with pI's ranging from 5.44 to 6.62. SCC Ag, a
immunoblotting using anti-TA-4 rabbit serum reveals that TA-4 consists
with protein (bovine) stabilizer. Minimum concentration: 0.07 μg/mL. Preservatives: Sodium Azide and other Antimicrobial Agents.
Other Reagents
ARCHITECT / Pre-Trigger Solution
• PRE-TRIGGER SOLUTION Pre-Trigger Solution containing 1.32% (w/v) hydrogen peroxide.
ARCHITECT / Trigger Solution
• TRIGGER SOLUTION Trigger Solution containing 0.35N sodium hydroxide.
ARCHITECT / Wash Buffer
• WASH BUFFER Wash Buffer containing phosphate buffered saline solution. Preservative: Antimicrobial Agent.

NAME
ARCHITECT SCC (Squamous Cell Carcinoma)
INTENDED USE
The ARCHITECT SCC assay is a Chemiluminescent Microparticle
Immunassay (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 6.82. SCC Ag, a
purified subfraction, has a pI of 6.82. 2 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
growth, detecting recurrence and monitoring disease status. 4-6 In other
types of squamous cell carcinoma (pharynx, larynx, palate, tongue and
neck), detectable but low serum TA-4 levels have been reported. 4,7
Crombach, et al. 8 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
epithelium and in squamous cell carcinoma of the exocervix than those
in normal columnar epithelium 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

BIOLICAL 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 System optics.

WARNING: SCC reactive determinants are shed naturally in saliva and
other body fluids. Contamination of the samples or the ARCHITECT
disposable washers, or oral 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 separtums. (Face masks are also
recommended.)
**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/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:
  - Sodium 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
- 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 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. 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). Specimens containing HAMA may produce anomalous values when tested with assay kits (such as ARCHITECT SCC) that employ mouse monoclonal antibodies.
- 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

<table>
<thead>
<tr>
<th>Sample Type</th>
<th>Endogenous SCC Added SCC</th>
<th>SCC Observed</th>
<th>Percent Recovery</th>
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<tr>
<td>Lot</td>
<td>Level (ng/mL)</td>
<td>(ng/mL)</td>
<td>(ng/mL)</td>
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<td>50.82</td>
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<tr>
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<td>3  0.44</td>
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<td>High Control</td>
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<td>50.64</td>
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<td>Panel 2</td>
<td>1  0.48</td>
<td>10.05</td>
<td>10.00</td>
</tr>
<tr>
<td></td>
<td>2  0.48</td>
<td>50.82</td>
<td>49.65</td>
</tr>
</tbody>
</table>

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.

| Sample Type | Endogenous SCC Added SCC Observed Percent Recovery |
|-------------|--------------------------|--------------|-----------------|
| Serum       | Level (ng/mL) | (ng/mL) | (ng/mL) | SD | CV | SD | CV |
| 1           | 0.38 | 10.09 | 10.35 | 98.8 |
| 2           | 0.38 | 52.53 | 49.53 | 93.6 |
| 3           | 0.35 | 10.09 | 10.67 | 102.3 |
| 4           | 0.35 | 52.53 | 52.48 | 99.2 |
| 5           | 0.37 | 10.09 | 10.90 | 104.4 |
|             | 0.37 | 52.53 | 51.10 | 96.6 |
|             | 0.25 | 10.09 | 10.14 | 98.0 |
|             | 0.25 | 52.53 | 48.29 | 91.5 |
|             | 0.31 | 10.09 | 10.48 | 100.8 |
|             | 0.31 | 52.53 | 51.65 | 97.7 |

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.

BIBLIOGRAPHY


