

BIO SYNEX® Bladder Tumor Antigen

A rapid test for the qualitative detection of bladder tumor antigen in urine. For professional *in vitro* diagnostic use only.

INTENDED USE

The BIO SYNEX® Bladder Tumor Antigen cassette test is a simple one step immuno-chromatographic assay for the rapid, detection of Bladder Tumor Marker in urine. Each test is used to obtain a qualitative result.

The BIO SYNEX® Bladder Tumor Antigen Test Device can be used as an aid to initiate or attend therapeutic treatments by physicians. Each device is designed for professional and *in-vitro* diagnostic.

INTRODUCTION

2-3% of all human malign tumors are bladder cancer tumors. After prostate carcinoma bladder cancer tumor comes in second of all tumors of the genitourinary system. Younger people are not so heavily concerned, the risk is increasing with age. Men are having a three times higher risk for this disease as women.

Certain exposures such as smoking, some chemicals and drugs stimulate the development of bladder cancer.

Established diagnostic methods to diagnose bladder tumors are urine cytology and cystoscopy. The disadvantage of urine cytology is a variable sensitivity; especially tumors in their early stages are often missed. Cystoscopy is not without risk because of its invasive nature furthermore will it only identify visible tumors.

Therefore a marker for diagnosis of bladder cancer has been searched in recent time. Bladder tumor protein concentration is elevated in urine samples of patients with bladder cancer. Elevated level of this protein is detected by BIO SYNEX® BLADDER TUMOR ANTIGEN-cassette test.

Several studies have confirmed that bladder tumor protein is a useful marker for the detection of bladder cancer. BIO SYNEX® BLADDER TUMOR ANTIGEN cassette test is an easy-to-use and patient friendly rapid test to diagnose and monitor bladder cancer.

TEST PRINCIPLE

The BIO SYNEX® Bladder Tumor Antigen cassette test employs a unique combination of monoclonal and polyclonal antibodies to selectively identify Bladder Tumor Protein in test samples with a high degree of sensitivity.

Bladder Tumor Protein-Antibodies are immobilized on the test region of the membrane. During the test, the specimen reacts with other Bladder Tumor Protein-antibodies conjugated to colored particles and precoated onto the sample pad of the test. The mixture then migrates through the membrane by capillary action and interacts with reagents on the membrane. If there is sufficient Bladder Tumor Protein in the specimen, a colored line will form at the test region of the membrane. The presence of this colored line indicates a positive result, while its absence indicates a negative result. The appearance of a colored line at the control region serves as a procedural control, indicating that proper volume of specimen has been added and membrane wicking has occurred.

MATERIALS PROVIDED

- Cassettes packed in individual pouch containing desiccant bag
- Pipettes
- Instructions for use

MATERIAL REQUIRED BUT NOT PROVIDED

- Timer
- Specimen collection container for urine samples collection

STORAGE AND STABILITY

The kit should be stored at 2-30°C until the expiry date printed on the box and test must remain in the sealed pouch until use.

Do not freeze.

Care should be taken to protect kit's components from contamination. Do not use if there is evidence of microbial contamination or precipitation. Biological contamination of dispensing equipment or containers can lead to false results.

PRECAUTIONS

- For professional *in vitro* diagnostic use only.
- For single use only.
- Do not use after stated expiration date.
- The test device should remain in the sealed pouch until use, because it is humidity sensitive!
- Therefore do not use test if pouch is damaged!
- Do not use more than the required amount of liquid.
- Use only urine as liquid and no other one instead.
- Do not spill the specimens into the reaction zone. Clean up spills thoroughly using an appropriate disinfectant.
- Avoid cross-contamination of urine samples by using a new specimen collection container and specimen pipette for each urine sample.
- Do not touch the reaction zone of the device to avoid contamination.
- Store and transport the test device always at 2-30°C (36°-86°F)
- Humidity and high temperature can adversely affect results.
- Do not eat, drink or smoke in the area where the specimens or kits are handled.
- Wear protective clothing such as laboratory coats, disposable gloves and eye protection when specimens are being tested.
- Urine specimens may be potentially infectious. Proper handling and disposal methods should be established.
- The components of the test (e.g. antibodies) do not cause any danger if the test is used according to the instructions.

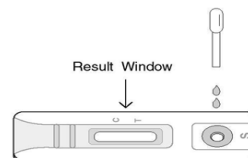
SPECIMEN COLLECTION AND HANDLING

1. Specimen collection should not be performed during or within three days of a menstrual period for female.
2. Only urine specimens should be used in this assay. Specimen should avoid contamination of toilet water.
3. Specimens collected, if not tested the same day, can be refrigerated and stored at 4 to 8 °C for testing up to 3 days after collection.

TEST PROCEDURE

1. Bring tests and specimens to room temperature (15-30°C) before use.
2. Remove the test panel from the foil pouch, and place it on a flat, dry surface. Label the test with patient or control identification. For best results, the assay should be performed within one hour.
3. Using the provided disposable pipette, transfer 2-3 drops of specimen to the specimen well (S) of the device (Figure above) and start the timer. Avoid trapping air bubbles in the specimen well (S), and do not add any solution to the result area.
4. As the test begins to work, color will migrate across the membrane. Wait for the colored line(s) to appear. The result should be read at 9 minutes. Do not interpret test results after 10 minutes.

Caution: The above interpreting time is based on reading the test results at room temperature of 15 to 30°C. If your room temperature is significantly lower than 15°C, then the interpreting time should be properly increased.



RESULTS

POSITIVE: Presence of 2 distinct colored lines: A control line appears at the level of the C zone and one colored line (**even of weak intensity**) appears at the level of the test T zone. A positive result indicates that Bladder Tumor Antigen has been detected.





NEGATIVE: Only one colored line appears at the level of the control line (C).

No line appears at the level of the test T zone. A negative result indicates that the specimen contains no Bladder Tumor Antigen



INVALID: No visible colored band at the level of control line C (whatever test line T apparition). Results from a test with no control line must be discarded. Review the procedure and repeat it with a new test device. If the problem persists, contact your local distributor.

Notes:

- The intensity of color in the test region (T) may vary depending on the concentration of analytes present in the specimen. Therefore, any color in the test region (T) should be considered positive. Note that this is a qualitative test, and cannot determine the concentrations of analytes in specimens.
- Once a positive result has been established (at 10 minutes), the result will not change. However, in order to prevent any incorrect results, the test result should not be interpreted after 10 minutes
- Insufficient specimen volume, incorrect operating procedure or expired tests are the most frequent reasons for control line failure.

QUALITY CONTROL

- Internal procedural controls are included in the test. A coloured line appearing in the control zone (C) ensures that sufficient specimen volume has been loaded and that the correct procedure has been followed by the operator.
- Good laboratory practices recommend the use of control materials to ensure proper kit performance. Control samples specific for this product are available separately.

LIMITATIONS OF PROCEDURE

- Specimen collection should not be performed during or within three days of a menstrual period for female.
- If a positive result is obtained with a patient taking aspirin, the test should be repeated after aspirin has been stopped for 7 days.
- A positive Bladder Tumor Antigen result indicate a likelihood of Bladder Cancer, however requires further confirmation.
- Negative results do not exclude bladder cancer. Other clinically available tests are required if questionable results are obtained. As with all diagnostic tests, a definitive clinical diagnosis should not be based on the results of a single test, but should only be made by the physician after all clinical and laboratory findings have been evaluated.
- The assay is designed for use with human urine only. Due to too low ionic strength (e.g. absence of ions) of some samples, it might be possible, that false results occur.

PERFORMANCES

Clinical study

A comparison study has been performed with cytology. A total of 225 patients with biopsy confirmed bladder cancer took part in this study. Of the 225 patients, stages were determined on 223, and grades are determined on 210 patients.

Stage	N	Sensitivity
Ta	14	57%
T1	69	82.6%
T2, T3	140	86.4%
Total	223	83.4%
Grade	N	
1	47	38.2%
2	61	63.9%
3	102	89.2%
Total	210	70.5%

Clinical Sensitivity:

The overall sensitivity varies between 70.5 % to 83.4% depending on the stages and grades of the bladder tumor. The sensitivity of the test varies from 38.2% (Grade 1) to 89.2% (Grade 3).

Analytical Specificity

Cross reactivity:

Positive and negative samples have been spiked with following substances:

- Acinetobacter calcoaceticus
- Neisseria catarrhalis

- Proteus vulgaris
- Salmonella typhi
- Acinetobacter spp
- Staphylococcus aureus
- Candida albicans
- Neisseria gonorrhoeae
- Escherichia coli
- Gardnerella vaginalis
- Neisseria meningitidis
- Streptococcus faecalis
- Neisseria lactamica
- Streptococcus faecium
- Pseudomonas aeruginosa
- Trichomonas vaginalis

None of the tested substances showed any cross-reaction with neither a clinically defined negative nor a positive specimen. Negative specimen samples with supplementation of potentially cross reacting substances gave consistently negative test results, whereas specimen samples positive to Bladder Tumor scored consistently positive.

Interferences:

Possible interfering substances were added to negative and positive urine samples with following amounts:

- Acetaminophene 20 mg/dl,
- Acetyl salicylic Acid 20 mg/dl,
- Ascorbic Acid 20 mg/dl,
- Atropine 20 mg/dl,
- Bilirubin 60 mg/dl,
- Caffeine 20 mg/dl,
- Creatinine 20 mg/dl,
- Gentesic Acid 20 mg/dl,
- Glucose 2000 mg/dl,
- Ketones 40 mg/dl,
- Mestranol 3 mg/dl,
- Nitrite 20 mg/dl,
- Penicillin 40,000 U/dl,
- Sodium Heparin 3 mg/dl,
- Lithium Heparin 3 mg/dl,
- LDL 200 mg/dL,
- Triglycerides 150 mg/dL

None of the tested substances showed any interference with neither a clinically defined negative nor a positive specimen. Negative specimen samples with supplementation of potentially interfering substances gave consistently negative test results, whereas specimen samples positive to Bladder Tumor scored consistently positive.

Literature

- Badrinath R. Konety and Robert H. Getzenberg: Urine based markers of urological malignancy. *The Journal of Urology*, Vol. 165, 600-611, Feb, 2001
- M-P Raitanen, E Kaasinen, E Rintala, E Hansson, P Nieminen, R Aine, TLJ Tammela1 and The Finn Bladder Group*: Prognostic utility of human complement factor H related protein test. *British Journal of Cancer* (2001) 85(4), 552-556
- Umiker W.: Accuracy of Cytologic Diagnosis of Cancer of the Urinary Tract. *Symposium on Diagnostic Accuracy of Cytologic Technics* 8:186-193,1964.
- Badalament R.A., Hermansen D.K., Kimmel M., Gay H., Herr H.W., Fair W.R., Whitmore W.F., Jr., Melamed M.R.: The Sensitivity of Bladder Wash Flow Cytometry, Bladder Wash Cytology, and Voided Cytology in the Detection of Bladder Carcinoma. *Cancer* 60:1423-1427, 1987.
- Robert-Koch Institut (Stand 1/2009) please refer to: http://www.rki.de/clin_100/nn_203956/DE/Content/GBE/Dachdok/Krebs/Broschuere/Lokalisationen/C67_D090_D414,templateId=raw,property=publicationFile.pdf/C67_D090_D414.pdf
- Sarosdy M.F., Hudson M.A., et al: Improved Detection of Recurrent Bladder Cancer Using the Bard BTA stat Test. *Urology* 50(3):349 - 353,1997.
- Raitanen M.-P., Marttila T., et al: The Bard BTA stat Test in Monitoring of Bladder Cancer. *The Journal of Urology* 157: 28, 1997.
- Kinders R., Jones T., et al: Complement Factor H or a Related Protein Is a Marker for Transitional Cell Carcinoma of the Bladder. *Clinical Cancer Research* 4:2511-2520, 1998.
- Corey M., Kinders R., et al: Factor H Related Proteins Are Upregulated In Bladder Cancer. *Proceedings of the American Association for Cancer Research* 39: 263, 1998.

SYMBOLS

- Attention, see instructions for use
- Lot number
- For *in vitro* diagnostic use only
- Manufacturer
- Store between 2-30°C
- Do not reuse
- Tests per kit
- Catalog number
- Expiry

Version 01 EN 01/2015



BIOSYNEX
12, rue Ettore Bugatti – CS28006
67038 STRASBOURG Cedex – France

Tél. : +33 3 88 77 57 00
Fax : +33 3 59 81 21 74

info@biosynex.com
www.biosynex.com