Interfering Substances

Positive and negative urine pools containing the substances listed below were tested using the NMP22 BladderChek Test.

Substance	Highest Level Tested with No Interference	Level at Which Substance Interfered
Whole blood	Up to 0.6% (v/v)	0.8% (v/v)[1]
Protein	Up to 100 mg/dL	No interference at MLT*
Glucose	Up to 20 mg/dL	No interference at MLT
Mitomycin C	Up to 10 mg/dL	No interference at MLT
Acetaminophen	Up to 20 mg/dL	No interference at MLT
Caffeine	Up to 20 mg/dL	No interference at MLT
Sodium acetylesalicylate	Up to 20 mg/dL	No interference at MLT
Sodium salicylate	Up to 20 mg/dL	No interference at MLT
Ibuprofen	Up to 20 mg/dL	No interference at MLT
Ampicillin	Up to 20 mg/dL	No interference at MLT
Sodium ascorbate (vit.C)	Up to 20 mg/dL	No interference at MLT
Nicotine	Up to 14 mg/dL	No interference at MLT
Sodium Chloride	Up to 365 mg/dL	No interference at MLT
Ethanol	Up to 1% (v/v)	No interference at MLT
Tetracycline	Up to 20 mg/dL	No interference at MLT
Trimethoprim	Up to 50 mg/dL	No interference at MLT
Flutamide	Up to 80 mg/dL	100 mg/dL[2]
Bilirubin, unconjugated	Up to 0.8 mg/dL	No interference at MLT
Nitrofurantoin	Up to 50 mg/dL	No interference at MLT
IgG	Up to 10 mg/dL	No interference at MLT
BCG	5 X 10^6 CFU	No interference at MLT
Uric Acid	Up to 250 mg/dL	No interference at MLT
Hemoglobin	Up to 100 mg/dL	No interference at MLT
E. coli	2.50E+10	No interference at MLT
P. aeruginosa	2.5E+12	No interference at MLT
C. albicans	1.25E+10	No interference at MLT
Cipro	100 mg/dL	125 mg/dL[3]
Levofloxacin	150 mg/dL	No interference at MLT
Isovue	1% (v/v)	No interference at MLT
Urised	17.5 mg/dL	No interference at MLT
Thiotepa	60 mg/dL	No interference at MLT
Finasteride	2.5 mg/dL	No interference at MLT
Phenazopyridine-HCl	72 mg/dL	80 mg/dL[4]
Doxorubicin HCl	Up to 10 mg/dL	No interference at MLT

*MLT: Maximum Level Tested

1. Positive interference: Substance increased the intensity of 0 and 5 U/ml urine panels to a positive result. This whole blood concentration represents 40X the threshold concentration for gross hematuria. This concentration is equal to 4.0 X 10^4 RBCs/µl of urine based on a calculated 5.0 X 10^6 RBCs/µl of blood.
2. Negative interference: Substance decreased the intensity of 15 U/mL urine panel to a negative result.
3. Substance gave invalid results for 0 and 5 U/mL urine panel members.
4. Substance's coloration caused all urine panel members' test results to be difficult to read.

The NMP22 BladderChek Test reported an interference with whole blood at 0.8% (v/v), Flutamide at 100 mg/dL, Cipro at 125 mg/dL, and phenazopyridine-HCl at 80 mg/dL. There was no interference with all other substances at the maximum level tested.

LIMITATIONS

Results of the NMP22 BladderChek Test should not be interpreted as absolute evidence for the presence or absence of bladder cancer. Any disease which could cause nuclear matrix proteins to be present in the urine may cause a positive test result. Positive results have been observed in some patients with benign urological diseases, prostate cancer, and active cancer treatment (see specificity table). The result from the NMP22 BladderChek Test should be used only in conjunction with information available from the clinical evaluation of the patient and other diagnostic procedures.

NMP22 BladderChek Test results should not be interpreted as evidence of the presence or absence of malignant disease in the bladder without corroboration from other diagnostic procedures. Other clinically accepted tests and procedures should be considered in the diagnosis of disease and good patient management. The effect of treatment with intravesical agents, such as BCG, Mitomycin C, Thiotepa, Bropirimine (investigational), or Interferon (investigational) is unknown.

The effects of experimental drugs on the NMP22 BladderChek Test is unknown.

Any modification by the laboratory to the test system or the FDA cleared test system instructions will result in the test no longer meeting the requirements for waived categorization. A modified test is considered to be high complexity until otherwise categorized and is subject to all applicable CLIA requirements contained in 42 CFR part 493.

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ORDERING and CONTACT INFORMATION

Catalog Number: D1200 contains 24 Determinations

To order:
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Technical Support

Further information can be obtained by contacting Abbott Technical Support:
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Symbols

2°C 30°C	Temperature limitation
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IVD	*In vitro* diagnostic medical device
	Consult instructions for use
℞ Only	Prescription Use Only
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www.globalpointofcare.abbott

IVD

PN: L0203 Rev. 9 2022/01

Abbott

NMP22™ BLADDERCHEK™ TEST

A Rapid Test for the Qualitative Detection of NMP22 Nuclear Matrix Protein in Human Urine.

This test is WAIVED under the Clinical Laboratory Improvement Amendments of 1988 (CLIA). If a laboratory modifies the test instructions, the test will no longer be considered waived.

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

℞ Only

INTENDED USE

The NMP22™ BladderChek™ Test is an *in vitro* immunoassay intended for the qualitative detection of the nuclear mitotic apparatus protein (NuMA), which is an abundant component of the nuclear matrix proteins, in urine of persons with risk factors or symptoms of bladder cancer or with a history of bladder cancer. This test is indicated for professional use and prescription home use as an aid in diagnosing and monitoring bladder cancer patients, in conjunction with standard diagnostic procedures.

CONTRAINDICATIONS, WARNINGS and PRECAUTIONS

Contraindications

- Test should not be used for individuals with indwelling urinary tract devices (such as stents) or who have had a total cystectomy.

Warnings And Precautions

- For *in vitro* diagnostic use only.
- Do not use beyond the printed expiration date.
- To avoid cross-contamination of samples, use a new dropper (provided with each device) for each patient urine.
- Treat urine samples and used devices as if they are potentially infectious.
- Do not reuse disposable test device. Discard after a single use.
- Refer to local regulations for the disposal of medical waste when disposing of any remaining kit components.
- Prior to opening the NMP22 BladderChek Test device package, inspect the packaging for rips, holes, or other openings. Should you encounter any such damage to the packaging, DO NOT USE THE DEVICE.
- To avoid erroneous results, use only plastic containers to process or store urine samples. Do not use glass, paper, foam, or any other type of collection container.

SUMMARY and EXPLANATION of the TEST

Bladder Cancer

The American Cancer Society estimates that there will be 61,420 new cases of bladder cancer, and approximately 13,060 deaths from this disease, in the United States in 2006.[1] The majority of bladder cancer cases occur in persons over 50 years of age, and over 70% of these cases occur in men. Diagnosis of cancers at an early stage has a dramatic impact on prognosis: the five-year survival rate for patients with bladder cancer is 94% if the tumor is diagnosed at a superficial stage; cancers detected when they are invasive or metastatic have five-year survival rates of 49% and 6% respectively.[1] Seventy-five to eighty percent of bladder tumors present as superficial disease (Ta, Tis, T1), and the majority of patients with superficial tumors (50-80%) will experience recurrence within six to twelve months. Approximately 10-20% of those tumors will progress in stage and grade. The predominant risk factors for recurrence are large tumor size, and high grade. Most commonly, recurrence is at the site of the original tumor resection, but there can also be developments of new tumor formations at other sites within the bladder.[2]

Cystoscopy

The standard for diagnosing patients for bladder cancer is cystoscopy. Precise incidence of false negative cystoscopy results in patients with bladder cancer is uncertain, but estimates range from 10-40%.[3-5] Sensitivity can be affected by poor visualization due to inflammatory conditions or bleeding, and flat urothelial lesions such as severe dysplasias and carcinoma *in situ* are frequently difficult to distinguish from normal bladder tissue.[6-7]

Voided Cytology

The sensitivity and specificity of urine cytology are largely dependent on the degree of differentiation of the tumor. Accuracy is reduced in lower grade tumors in which the cytologic features of the neoplastic cells deviate less from the normal, and may overlap with some inflammatory or traumatically induced conditions. In addition, small and/or well-differentiated (low grade) papillary tumors are less likely to exfoliate cells spontaneously because the strong intercellular attachments are better preserved.[8] Sensitivity in detection of low grade lesions is reported as only 16-30%.[6,9-13] Because the interpretation of cytology samples requires trained personnel, the urine must be sent to a laboratory. Results may take 24 hours or more to be returned to the physician, and therefore the urine cytology results may not be available during the cystoscopy visit.

The detection of bladder cancer could be improved with a rapid, simple, urine test, so that the physician has the results available before performing cystoscopy. The NMP22 BladderChek Test is a single-step, antibody-based test that is performed in only 30 minutes with no pretreatment of the urine sample.

Nuclear Matrix Proteins

Nuclear matrix proteins (NMPs) make up the internal structural framework of the nucleus[14-15] and are associated with such functions as DNA replication, RNA synthesis, and hormone binding.[16-17] Further work has indicated that NMPs are involved in regulation and coordination of gene expression.[18-20] Research by Fey and Penman demonstrated that NMP expression varied with cell type of origin.[21]

Nuclear mitotic apparatus protein (NuMA) is an abundant component of the nuclear matrix proteins (NMPs). It is dispersed within the nucleus during interphase and localizes with the spindle poles during mitosis. Nuclear mitotic apparatus protein was originally described by Lydersen and Pettijohn in analyses of non-histone chromatin proteins.[22] Subsequently, other functions have been proposed for nuclear mitotic apparatus protein, including maintenance of nuclear structure, establishment/maintenance of the mitotic spindle and re-formation of the nucleus after mitosis.[23]

Structurally, this 240 kD nuclear mitotic apparatus protein contains globular head and tail domains separated by a central helical rod region. The cDNA for nuclear mitotic apparatus protein has been cloned and sequenced by several different groups, although sequence discrepancies have been reported.[24-26]

In tumor cells, nuclear mitotic apparatus protein is elevated concordant with the structural/morphological changes characteristic of malignant cell nuclei. The protein is released from cells in detectable levels as a result of cell death (e.g. apoptosis). Nuclear mitotic apparatus protein that has been released from bladder tumor cells is measured in urine using monoclonal antibodies that recognize specific domains of the protein. The nuclear mitotic apparatus protein antigen moiety detected by the NMP22 BladderChek Test is referred to as NMP22.

PRINCIPLE of the PROCEDURE

The NMP22 BladderChek Test technology uses a lateral flow immunochromatographic strip encased in a plastic cartridge to detect nuclear matrix protein qualitatively in the patient's urine sample. The antibodies in the lateral flow immunochromatogaphic strip are monoclonal antibodies (MAbs) raised against NuMA extracted from a cervical cancer cell line by the method of Fey and Penman.[21] Two different MAbs are used, one as a capture antibody and one as a reporter antibody.

Unprocessed voided urine is added to the sample well of the cartridge and allowed to react for 30 minutes. There are no other procedural steps. If the antigen is present in the urine, it will interact with the colloidal gold conjugated particles to form an immune complex. The reaction mixture flows through the membrane, which contains zones of immobilized antibodies. In the Test (T) zone, antigen-conjugate complexes are trapped by the capture antibody, forming a visible line if the concentration of antigen in the urine is elevated. The procedural Control (C) zone contains an immobilized goat anti-mouse IgG-specific antibody that will capture the colloidal gold conjugated antibody, thereby producing a visible line in the Control window. This procedural control assures the operator that each device is working properly, independently of the presence or absence of the antigen in the urine sample.

DEVICES and REAGENTS

The NMP22 BladderChek Test is individually packaged in a sealed foil pouch with a urine dropper and a desiccant. Each device incorporates colloidal gold particles conjugated to the reporter antibody and a capture monoclonal antibody, immobilized on a membrane. The procedural Control zone contains an immobilized goat anti-mouse IgG-specific antibody.

MATERIALS REQUIRED but NOT PROVIDED

- Plastic urine collection container. Do not use paper or foam cups.
- Watch or timer

STORAGE and STABILITY

Store the NMP22 BladderChek Test at 2-30 °C. Do not freeze. The device is stable when stored at these temperatures until the printed expiration date.

SPECIMEN COLLECTION, STORAGE, and PREPARATION

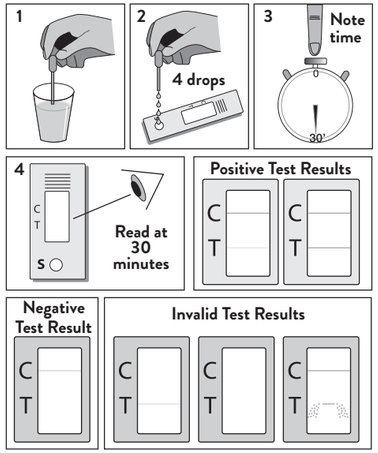
Voided urine is required for the NMP22 BladderChek Test. Bladder barbotage specimens, catheterized urine specimens, serum, plasma, or whole blood should not be used. Urine should be collected without preservatives or fixatives in a clean urine cup and labeled appropriately. If urine is to be used for other tests, remove an aliquot of the specimen (a minimum of 2 ml) for this test to avoid contamination. Urine samples may be stored at room temperature for up to 2 hours after collection.

- This test should not be used on individuals with indwelling urinary tract devices (such as stents) or who have had a total cystectomy.
- Use only plastic containers for urine collection. Do not use paper or foam cups.
- Collection of urine during active chemo-, immuno-, or radiation therapy may cause positive results.
- Some patients with active prostate cancer may yield positive results with the NMP22 BladderChek Test.
- For trauma to the bladder or urinary tract due to surgery, biopsy, etc., the physician should allow ample time for trauma recovery before using the test.

PATIENT TEST PROCEDURE

1. Collect a voided urine sample in a plastic urine collection container.
2. Keep the urine sample at room temperature until time of testing. Do not refrigerate or freeze the urine sample.
3. Test the patient urine sample within 2 hours of collection.
4. Inspect the device packaging for perforations or tears. If damaged, do not use.
5. If test is stored refrigerated, bring the test materials to room temperature (18-30°C, 64-86°F) before opening the package.
6. Remove the test device and dropper from foil package immediately prior to use. Throw away the small desiccant pouch.
7. Fill the dropper provided with the patient's urine sample and hold it upright above the sample well.
8. Allow 4 FULL drops (without air bubbles) to fall into the sample well.
9. Read the test result at 30 minutes, but NO LATER THAN 50 MINUTES. Test results are not valid if read later than 50 minutes. Read results as shown under "Interpretation of Results."
10. Discard used dropper and test device in a proper biohazard container.

INTERPRETATION of RESULTS



1. Check the procedural Control (C) window. A line must appear for the test to be valid.
2. **Positive Result:** Carefully observe the Test (T) area of the device. **ANY complete** line in the Test (T) area is a POSITIVE result when a Control (C) line is present. Neither the intensity nor the color of the Test (T) line should be compared to that of the line in the procedural Control (C) area.
3. **Negative Result:** Carefully observe the Test (T) area of the device. The absence of any colored line in the Test (T) area is a NEGATIVE result if a Control (C) line is present.
4. **Invalid Result:** If no line appears in the procedural Control (C) area, or if the Test (T) line is smeared or incomplete, the test is INVALID and must be repeated with a new device. The most common reason for an invalid result is failure to add exactly 4 FULL drops, without air bubbles, of urine to the sample well.

QUALITY CONTROL

Good laboratory practices recommend the use of appropriate controls. There is an internal procedural control for the NMP22 BladderChek Test.

Procedural Control

The procedural Control is found in the Control (C) zone of the test device. This control assures the operator that (1) sample addition and migration through the device has occurred and that (2) the control goat anti-mouse antibody and the colloidal gold conjugated reporter monoclonal antibody are intact and functional. This control does not ensure that the Test (T) zone is accurately detecting the presence or absence of antigen in the sample.

External Controls

Positive and Negative external controls are available separately in the NMP22 BladderChek Control Kit (catalog #D1250). The external controls test for the presence and reactivity of the capture and conjugated monoclonal antibodies in a test device. To obtain external controls, contact Customer Service or your local distributor.

It is recommended that external controls be tested at the following times:

1. Whenever laboratory or room conditions have been above 30 °C if stored at room temperature.
2. To perform training or retraining of testing personnel.
3. Whenever NMP22 BladderChek Test results do not match other clinical findings or symptoms.

Good laboratory practices include a complete quality control program. This entails proper sample collection and handling practices, ongoing training of testing personnel, ongoing evaluation of control results, proper storage of test kits, etc. A permanent record of control results should be retained.

EXPECTED RESULTS

Clinical Performance for Diagnosis

A prospective clinical trial was performed at 22 sites to determine the utility of NMP22 BladderChek Test as an aid in diagnosing patients with risk factors or symptoms of bladder cancer. Voided urine samples were collected from 1331 patients prior to cystoscopy, and clinical staff performed the testing. Physicians conducting the cystoscopies were blinded to the device results.

To determine the sensitivity and specificity, patients were classified as positive or negative for bladder cancer. Patients were considered negative if no tumor was seen endoscopically, or, if a lesion was seen, was pathologically determined to be non-malignant. There were 682 patients diagnosed as having benign disease(s), and 567 with no evidence of urinary tract disease. Patients were considered positive for bladder cancer if a tumor was seen during cystoscopy, and, if removed was pathologically determined to be malignant. There were 82 neoplasms, of which 75 were resected and had staging information. Grade was available for 70 of the cancers. The remaining 7 patients did not undergo surgical removal, and therefore their tumors could not be staged or graded (Tx, Gx). Patients with active cancers other than of the bladder were recruited at a single site.

Specificity for individuals with no evidence of disease, benign disease by group, history of non-bladder cancer, and active cancers other than of the bladder is presented in the following table.

	Specificity	(95% CI)
Patients with No Evidence of Disease (Risk factor or symptom)	90.3% (512/567)	(87.6%, 92.6%)
Benign Diseases*		
BPH/prostatitis	82.5% (231/280)	(77.5%, 86.8%)
Cystitis/inflammation/trigonitis/UTI	77.6% (97/125)	(69.3%, 84.6%)
Erythema	82.4% (42/51)	(69.1%, 91.6%)
Hyperplasia/squamous metaplasia/ cysts and polyps	76.9% (40/52)	(63.2%, 87.5%)
Calculi	72.5% (29/40)	(56.1%, 85.4%)
Trabeculations	80.7% (175/217)	(74.7%, 85.7%)
Other benign diseases, kidney and genitourinary	81.4% (179/220)	(75.6%, 86.3%)
Cancer History, non-bladder – Inactive Other Cancers^	87.5% (7/8)	(47.3%, 99.7%)
Cancer History, non-bladder – Active Other Cancers^^	86.8% (33/38)	(71.9%, 95.6%)

*Patients may have more than one benign disease

^ History: lung (1/1), prostate (6/7)

^^ Active: breast (13/14), kidney/renal (3/5), leukemia/lymphoma (3/3), lung (1/1), prostate (10/12), other (3/3, tongue, testes, spindle-cell (flank))

Sensitivity for patients with bladder cancer (Ta-Tx) was 55.7%. Patients were considered positive for bladder cancer if a tumor was seen during flexible or rigid cystoscopy, and, if removed, was pathologically determined to be malignant.

NMP22™ BLADDERCHEK™ Test	Cystoscopy		
	Negative	Positive	Total
Negative	1070	38	1108
Positive	179	44	223
Total	1249	82*	1331

*Includes tumors T0-Tx

Overall sensitivity (Ta-Tx) and specificity for the clinical trial was as follows.

	Sensitivity (95% Exact CI)	Specificity (95% Exact CI)	Positive Predictive Value (95% Exact CI)	Negative Predictive Value (95% Exact CI)
NMP22™ BLADDERCHEK™ Test vs Cystoscopy	55.7% (44.1%, 66.9%) (44/79)	85.7% (83.6%, 87.6%) (1070/1249)	19.7% (14.7%, 25.6%) (44/223)	96.8% (95.6%, 97.8%) (1070/1105)

The NMP22 BladderChek Test was more sensitive to later stages and higher grades of cancer, although the majority of malignancies were non-invasive. Sensitivity by stage and grade is detailed in the table below.

	Sensitivity of NMP22™ BLADDERCHEK™ Test	(95% CI)
Tumor stage: Ta- T1	50.0% (31/62)	(37.0%, 63.0%)
Tumor stage: T2- T3	90.0% (9/10)	(55.5%, 99.8%)
Tumor stage: Tx	57.1% (4/7)	(18.4%, 90.1%)
Tumor grade: Well differentiated (Grade 1)	48.2% (13/27)	(28.7%, 68.1%)
Tumor grade: Moderately differentiated (Grade 2)	50.0% (9/18)	(26.0%, 74.0%)
Tumor grade: Poorly differentiated (Grade 3 or Grade 4)	72.0% (18/25)	(50.6%, 87.9%)
Tumor grade: Gx (Grade unknown)	44.4% (4/9)	(13.7%, 78.8%)

The incidence rate for bladder cancer in this study was 5.9%. The following table demonstrates the Positive (PPV) and Negative (NPV) predictive values of the NMP22 BladderChek Test at varying incidence rates.

Incidence Rate	NMP22™ BLADDERCHEK™ Test Sensitivity †=55.7% Specificity=85.7%	
	PPV	NPV
1%	3.8%	99.5%
5.9%*	19.7%	96.8%
7%	22.7%	96.3%
15%	40.7%	91.6%

†Bladder cancers used in calculations: Ta-Tx

*Actual incidence rate from NMP22 BladderChek Test Diagnosis Study

Clinical Performance for Monitoring

A prospective clinical trial was performed at 23 sites to determine the utility of NMP22 BladderChek Test as an aid in monitoring patients with a history of bladder cancer. Voided urine samples were collected from 668 patients prior to surveillance cystoscopy, and clinical staff performed the testing. Physicians conducting the cystoscopies were blinded to the device results.

To determine the sensitivity and specificity, patients were classified as positive or negative for bladder cancer. Patients were considered negative if no tumor was seen endoscopically, or, if a lesion was seen, was pathologically determined to be non-malignant. There were 291 patients diagnosed as having benign disease(s), and 279 with no evidence of urinary tract disease. Patients were considered positive for bladder cancer if a tumor was seen during cystoscopy, and, if removed, was pathologically determined to be malignant. There were 98 recurrences of neoplasms, of which 61 were resected and had stage and grade information available. The remaining 37 patients did not undergo surgical removal, and therefore their tumors could not be staged or graded (Tx, Gx).

Specificity for individuals with no evidence of disease, benign disease by group, history of non-bladder cancer, and active cancers other than of the bladder is presented in the following table.

	Specificity	(95% CI)
Patients with No Evidence of Disease (History of Bladder Cancer)	83.9% (234/279)	(79.0%, 88.0%)
Benign Diseases*	**Specificity**	**(95% CI)**
BPH/prostatitis	89.6% (120/134)	(83.1%, 94.2%)
Cystitis/inflammation/trigonitis/UTI	85.2% (23/27)	(66.3%, 95.8%)
Erythema	92.5% (49/53)	(81.8%, 97.9%)
Hyperplasia/squamous metaplasia/ cysts and polyps	82.4% (14/17)	(56.6%, 96.2%)
Calculi	100% (5/5)	(47.8%, 100%)
Trabeculations	89.1% (106/119)	(82.0%, 94.1%)
Other benign diseases, kidney and genitourinary	86.4% (51/59)	(75.0%, 94.0%)
Cancer History, non-bladder – Inactive Other Cancers^	88.8% (71/80)	(79.7%, 94.7%)
Cancer History, non-bladder – Active Other Cancers^^	71.4% (5/7)	(29.0%, 96.3%)

***Patients may have more than one benign disease**

^ Types of cancers: prostate (n=29), skin (n=18), kidney/renal (n=15), genitourinary, non-bladder, non-prostate (n=5), breast (n=6), GI (n=6), lung/respiratory (n=4), blood (n=1), other (n=3)

^ Patients may have more than one type of prior cancer, and current benign diseases.

^^ Types of cancers: prostate (2/4), 1 kidney (0/1), 1 cervical (0/1), 1 lung/liver (0/1)

Sensitivity for patients with bladder cancer was 45.9%. Patients were considered positive for bladder cancer if a tumor was seen during cystoscopy, and, if removed, was pathologically determined to be malignant.

NMP22™ BLADDERCHEK™ Test	Cystoscopy		
	Negative	Positive	Total
Negative	492	53	545
Positive	78	45	123
Total	570	98	668

Overall sensitivity and specificity for the clinical trial was as follows.

	Sensitivity (95% Exact CI)	Specificity (95% Exact CI)	Positive Predictive Value (95% Exact CI)	Negative Predictive Value (95% Exact CI)
NMP22™ BLADDERCHEK™ Test vs Cystoscopy	45.9% (35.8%, 56.3%) (45/98)	86.3% (83.2%, 89.0%) (492/570)	36.6% (28.1%, 45.8%) (45/123)	90.3% (87.5%, 92.6%) (492/545)

The NMP22 BladderChek Test was more sensitive to later stages and higher grades of cancer, although the majority of malignancies were non-invasive. Sensitivity by stage and grade is detailed in the next table.

	Sensitivity of NMP22™ BLADDERCHEK™ Test	(95% CI)
Tumor stage: Ta- T1	40.0% (22/55)	(27.0%, 54.1%)
Tumor stage: T2- T3	80.0% (4/5)	(28.4%, 99.5%)
Tumor stage: Tx	51.4% (19/37)	(34.4%, 68.1%)
Tumor grade: Well differentiated (Grade 1)	30.0% (9/30)	(14.7%, 49.4%)
Tumor grade: Moderately differentiated (Grade 2)	33.3% (4/12)	(9.9%, 65.1%)
Tumor grade: Poorly differentiated (Grade 3 or Grade 4)	66.7% (12/18)	(41.0%, 86.7%)
Tumor grade: Gx (Grade unknown)	52.6% (20/38)	(35.8%, 69.0%)

The incidence rate for bladder cancer recurrence in this study was 14.7%. The following table demonstrates the Positive (PPV) and Negative (NPV) predictive values of the NMP22 BladderChek Test at varying incidence rates.

Incidence Rate	NMP22™ BLADDERCHEK™ Test Sensitivity †=45.9% Specificity=86.3%	
	PPV	NPV
10%	27.1%	93.5%
14.7%*	36.6%	90.3%
20%	45.6%	86.5%
30%	58.9%	78.8%

* Actual incidence rate from NMP22 BladderChek Test Monitoring Study

Concordance of NMP22 BladderChek Test and NMP22 Test Kit (microplate).

In comparison testing using voided urine samples, the NMP22 BladderChek Test showed good concordance with the NMP22 Test Kit (microplate).

Voided urine samples were collected from 217 individuals at urology clinics. An aliquot of each sample was applied to an NMP22 BladderChek Test device. An additional aliquot was stabilized immediately and tested by the NMP22 Test (microplate) to quantify the NMP22 antigen concentration.

Overall concordance was 91.2% (198/217, CI 86.7%, 94.7%), with a positive concordance of 87.0% (20/23, CI 66.4%, 97.2%) and negative concordance of 91.8% (178/194, CI 86.9%, 95.2%).

	NMP22™ BLADDERCHEK™ Test		
NMP22 Microplate Assay	**Negative**	**Positive**	**Total**
Negative (≤ 10 U/mL)	178	16	194
Positive (> 10 U/mL)	3	20	23
Total	181	36	217

PERFORMANCE CHARACTERISTICS

Reproducibility by Laboratory Technicians

Precision studies were conducted to determine the percent of devices correctly read. Specimen panels with NMP22 levels of 0, 5, 15, and 25 U/mL were used. Three laboratory technicians each read ten devices per level in random order, (40 devices/lab tech) for five different days. This produced 150 individual reads per panel level (3 readers x 10 devices per panel x 5 days). The experiment was conducted on three separate lots of devices.

The percent of correctly read NMP22 BladderChek Test devices was very consistent across lots (n=3), lab techs (n=3), and days (n=5), where urine specimens with NMP22 antigen levels of 0 and 5 U/mL should have been read as negative and urine specimens with NMP22 antigen levels of 15 and 25 U/mL should have been read as positive.

The overall percent of correct reads was 99.2% (1786/1800). Twelve of the 14 incorrect results were at 5 U/mL (438/450 or 97%), which could be expected near the test cut-off.

Reproducibility by Lay Users Compared to Professional Readers

A precision study with a three-level precision panel of prepared samples was also conducted to evaluate lay user reproducibility. The three levels were targeted to the concentrations of 2, 10 and 15 U/mL to represent negative, low positive and positive values. Five lay readers each conducted assays on two blinded and randomized aliquots of the above samples, resulting in a total of ten results per level. In addition, two professional readers each tested five blinded and randomized replicates of the three-level precision panel, producing ten results for each level. There was 100% concordance among the lay readers, between the professional readers, and between the lay and professional readers. All samples at 2 U/mL were read as negative, and all samples at 10 and 15 U/mL were read as positive.

Performance of Lay Users Compared to Professionals

Field studies to evaluate the ability of lay users compared to professional users of the NMP22 BladderChek Test were conducted at three locations. Each volunteer, aged 50 years or older, some with a history of bladder cancer, tested his or her own urine with one device. At each site professional medical staff re-read the devices used by the lay users, and also conducted their own testing of the volunteers' samples using new devices. To ensure the presence of some positive results in the study, fourteen samples were spiked with NMP22 antigen to approximately 15 U/mL and fourteen with approximately 25 U/mL. In addition, eight devices were made invalid by not having a working control line.

There was an overall 96.4% concordance between the results obtained by lay users and professional staff reading the same device, and 95.6% agreement between professional and lay users testing the same urine sample on different devices. All spiked specimens were read correctly by lay and professional readers.

	Percent Overall Concordance with Lay User Result			
	Site 1 (N=55)	Site 2 (N=35)	Site 3 (N=47)	Overall (N=137)
Professional Re-testing of same urine sample with new NMP22™ BladderChek™ Test	96.4% (53/55)	97.1% (34/35)	93.6% (44/47)	95.6% (131/137)
Professional Re-Read of Lay-User NMP22™ BladderChek™ Test	96.4% (53/55)	100% (35/35)	93.6% (44/47)	96.4% (132/137)

High Dose Hook Effect

High dose hook (prozone) effect tests were conducted to determine if the NMP22 BladderChek Test is free from interference from high concentration positive patient samples. Results showed that there was no prozone effect up to 10,000 U/mL NMP22 antigen in a patient's urine sample, which was the highest concentration tested.

Abbott
NMP22
Bladdercheck Test

Package Insert, US

Size:
17 in x 11 in

Black

PN: L0203
Rev: 9

Date of Last Revision:
9.9 2022/01/26