JUL 3 0 2002

510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: K021231

Name: Matritech, Inc.
330 Nevada St.
Newton, MA 02460

Contact: Melodie R. Domurad PhD
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Date: April 15, 2002

Catalog Number: D1200 24-test kit
D1201 1-test kit
D1250 Control kit

Device Name: NMP22® BladderChek™ Kit
NMP22® Control Kit

Common: NMP22 BladderChek

Classification: Class II

Manufacturer: Unotech Diagnostics, Inc.
2235 Polvorosa Ave.
Suite 220
San Leandro, CA 94577

Registration Number: 1225597 Matritech, Inc.
2953160 Unotech Diagnostics, Inc.

Substantially Equivalent Predicate Device: BTA *Stat* Test

Description of Device

The NMP22 BladderChek Test is an *in vitro* diagnostic assay for the qualitative detection of the nuclear matrix protein NMP22 in human urine.

Intended Use

The Matritech NMP22 BladderChek Test is indicated for professional and prescription home use as an aid in monitoring bladder cancer patients, in conjunction with standard diagnostic procedures.

Summary and Explanation of the Test

The NMP22 BladderChek Test for nuclear matrix protein NMP22 is an immunochromatographic assay utilizing monoclonal antibodies in a lateral flow strip encased in plastic. Two different antibodies are used, one as a capture and one as a reporter antibody. Unprocessed patient urine is added to the sample well of the cartridge and allowed to react with the colloidal gold conjugated reporter antibody. If the antigen is present in urine, it will interact with the reporter conjugate 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 urine is elevated. The procedural Control (C) zone contains an immobilized goat anti-mouse IgG-specific antibody that will capture the conjugated antibody independently of the presence or absence of the antigen, thereby always producing a visible line in the Control window. This procedural control assures the operator that each device is working properly.

Substantial Equivalence to Predicate Device

Both the NMP22 BladderChek Test and BTA *Stat* are single use, *in vitro* diagnostic devices for detecting recurrence in patients with a history of bladder cancer. The assay reactions for the two devices are immunochromatographic, utilizing monoclonal antibodies, and produce qualitative results. Both detect analytes from voided urine. Targeted environment for the two tests is prescription home use. The NMP22 BladderChek Test detects the nuclear matrix protein NMP22, and the BTA *Stat* Test detects Bladder Tumor Antigen.

	NMP22 BladderChek K021231	BTA *Stat* K974845 & K964151
Intended Use	Aid in the monitoring of bladder cancer patients in conjunction with standard diagnostic procedures	Aid in the management of bladder cancer patients in conjunction with cystoscopy
Sample Matrix	Voided urine	Voided urine
Procedural Steps	Add 4 drops of urine	Add 5 drops of urine
Result Interpretation	+/-, Qualitative	+/-, Qualitative
Analyte Measured	NMP22 Nuclear Matrix Protein	BTA Bladder Tumor Antigen
Targeted Environment	Professional and Prescription Home Use	Laboratory and Prescription Home Use
Assay Reaction	Immunochromatographic	Immunochromatographic

Non-Clinical Tests

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 devices was very consistent across lots (n=3), lab techs (n=3), and days (n=5), where urine specimens with NMP22 levels of 0 and 5 U/mL should have been read as negative and urine specimens with NMP22 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 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 10 results for each level. There was 100% concordance among the lay readers, between 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 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 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™ Device	96.4% (53/55)	97.1% (34/35)	93.6% (44/47)	95.6% (131/137)
Professional Re-Read of Lay User NMP22 BladderChek™ Device	96.4% (53/55)	100% (35/35)	93.6% (44/47)	96.4% (132/137)

Clinical Tests

A prospective clinical trial was performed at 23 sites to determine the utility of NMP22 BladderChek 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*		
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.

Cystoscopy	NMP22 BladderChek Test		
	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 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 table below.

	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 Monitoring Study

Concordance of NMP22 BladderChek 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 a BladderChek Test device. An additional aliquot was stabilized immediately and tested by the Matritech NMP22 (microplate) Test Kit to quantify the NMP22 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 Microplate Assay	NMP22 BladderChek Test		
	Negative	Positive	Total
Negative (≤10 U/mL)	178	16	194
Positive (> 10 U/mL)	3	20	23
Total	181	36	217

Conclusion

The NMP22 BladderChek Test and its predicate device, the BTA *Stat* are technologically similar. The assay reactions (immunochromatography utilizing monoclonal antibodies), sample matrix (voided urine), procedural steps (addition of drops of urine to device), result interpretation (qualitative +/-), patient population (history of bladder cancer), and indication (aid in monitoring), are all similar.

Reproducibility of results with NMP22 BladderChek were excellent between laboratory technicians across lots, days and specimen panel levels. Overall percent of correct reads was 99.2%. A precision study using a prepared specimen panel of negative (2 U/mL), low positive (10 U/mL) and positive (15 U/mL) samples demonstrated 100% concordance between professional staff (n=2) and lay users (n=5). In addition, an investigation to evaluate performance of lay users compared to professional readers showed 96.4% overall concordance when professionals re-read tests performed by lay volunteers using their own urine, and 95.6% when the professionals re-tested the lay users' urine samples. The BTA *Stat* package insert states that reproducibility studies were performed to determine day-to-day, reader-to-reader, lot-to-lot, and laboratory-to-laboratory variability. It reports that these studies showed nearly total agreement with the exception of samples near the limit of detection, thus non-clinical performance of the two devices is comparable.

In the prospective clinical trial performed with NMP22 BladderChek sensitivity was 45.9% (CI 35.8%, 56.3%) and specificity was 86.3% (CI 83.2%, 89.0%), with a positive predictive value of 36.6% (CI 28.1%, 45.8%) and a negative predictive value of 90.3% (CI 87.5%, 92.6%). The incidence rate of cancer in the study population was 14.7%. Per its package insert, BTA *Stat* demonstrated 67% (CI 60%, 73%) sensitivity and 70% (CI 61%, 79%) specificity. Because the performance for this device was determined using retrospective samples selected from a frozen bank, incidence rate could not be determined, so true positive and negative predictive values could not be calculated.

Using a range of theoretical incidence rates of 10%, 20% and 30%, the NMP22 BladderChek Test demonstrated positive predictive values of 27.1% to 58.9%, compared to 19.8% to 48.8% for BTA *Stat*. In addition, the overall accuracy (defined as test positive for patients with cancer and test negative for patients without cancer divided by the total number of patients) of NMP22 BladderChek was 80.3% compared to 67.9% for BTA *Stat*. This was due in part to the excellent specificity of BladderChek, resulting in fewer false positive results.

The non-clinical and clinical studies presented in this submission demonstrate that the clinical utility and performance of NMP22 BladderChek is equivalent or better than that of the predicate device, BTA *Stat*.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUL 3 0 2002

Melodie R. Domurad, Ph.D.
Vice President, Clinical and Regulatory Affairs
Matritech, Inc.
330 Nevada Street
Newton, Massachusetts 02460

Re: k021231
Trade/Device Name: NMP22® BladderChek™ Test
Regulation Number: 21 CFR § 866.6010
Regulation Name: Tumor Marker Test Systems – Monitoring-Bladder
Regulatory Class: II
Product Code: MMW
Dated: June 27, 2002
Received: June 28, 2002

Dear Dr. Domurad:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

INDICATION FOR USE STATEMENT

510(k) Number: K 021231 K021231

Device Name: NMP22® BladderChek™ Test

Indication For Use:

The NMP22 BladderChek test is indicated for use as an aid in monitoring bladder cancer patients, by professional and prescription home use, in conjunction with standard diagnostic procedures.

J P Reeves for S. Altaie

(Division Sign-Off)
Division of Clinical Laboratory Devices

510(k) Number K021231

(PLEASE DO NOT WRITE BELOW THIS LINE CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Prescription Use (Per 21 CFR 801.109)) OR Over-The Counter Use