Summary of Safety and Effectiveness Data

I. General Information

Device Generic Name:	Immunoassay for the *in vitro* quantitative determination of free prostate specific antigen (PSA) in human serum
Device Trade Name:	Dimension® FPSA Flex® Reagent Cartridge Dimension® T/F PSA Calibrator
Applicant's Name and Address:	Dade Behring, Inc. P.O. Box 6101 Newark, DE 19714
Premarket Approval Application (PMA) Number:	P020027
Date of Panel Recommendation:	Refer to section XII
Date of Good Manufacturing Practice Inspection:	April 5 to 9, 2002
Date of Notice of Approval to the Applicant:	January 24, 2003

II. Indications for Use

The FPSA method for the Dimension® clinical chemistry system with the heterogeneous immunoassay module is an *in vitro* diagnostic test intended to quantitatively measure free prostate specific antigen (FPSA) in human serum. Measurements of FPSA are used in conjunction with total PSA (TPSA) method on Dimension® system to calculate FPSA to TPSA ratio expressed as a percent FPSA. The percent FPSA is used as an aid in distinguishing prostate cancer from benign prostate conditions in men 50 years or older with TPSA of 4.0 to 10.0 ng/mL [µg/L] and digital rectal examination (DRE) findings not suspicious for cancer. Prostate biopsy is required for diagnosis of cancer.

The Dimension® Total/Free (T/F) PSA Calibrator is intended for use with the Dimension® Free PSA Flex® reagent cartridge and the Dimension® TPSA Flex® reagent cartridge.

III. Contraindications

There are no known contraindications for the .Dimension® FPSA Flex® reagent cartridge.

IV. Warnings and Precautions

Refer to the product labeling for a list of warnings and precautions.

V. Device Description

A. Test Principle

The Dimension® FPSA Flex® reagent cartridge is a solid phase, two-site, one step enzyme immunoassay for use on the fully automated random access analyzer, the Dimension® RxL clinical chemistry system with the Heterogeneous Immunoassay module. Serum sample containing FPSA is incubated with chromium dioxide particles (CrO_2) coated with anti-FPSA monoclonal antibody and the conjugate reagent, β-galactosidase labeled anti-PSA monoclonal antibody. During incubation, a CrO_2-Ab /PSA/conjugate sandwich is formed. Unbound conjugate and analyte are removed by magnetic separation and washing. In the presence of the chromogenic substrate chlorophenol red-β-d-galactopyranoside (CPRG), the sandwich bound β-galactosidase will hydrolyze the CPRG to chlorophenol red (CRP). The color change is measured at 577 nm and is directly proportional to the concentration of PSA present in the sample. The amount of FPSA in the sample is determined from a standard curve generated by the Dimension® T/P calibrators.

B. Kit Description

The Dimension® FPSA Flex® reagent cartridge for the Dimension® clinical chemistry system with heterogeneous immunoassay module has been designed for use with the Dimension® RxL and Xpand™ systems. The Dimension® FPSA Flex® reagent cartridge is a plastic (high–density polyethylene) molded part designed to provide eight separate wells. All reagents required for the assay (PSA Ab- β-galactosidase, Chrome diluent, PSA Antibody-CrO_2 tablet, CPRG tablet and CPRG diluent) are contained separately within these wells. Each cartridge has a barcode label used for automatic transfer of information to the Dimension® RxL clinical chemistry system when the cartridge is loaded onto the instrument. This information includes the method name, lot number, Flex® reagent cartridge sequence number and expiration date.

C. Calibrator Kit Description

The Dimension® T/F PSA calibrator is a six level liquid product packaged and sold separately from the Dimension® FPSA Flex® reagent cartridge. Each box contains two vials of each level. Level 1 is a horse serum base with no detectable PSA. Levels 2, 3, 4, 5 and 6 are formulated in a 6% bovine albumin matrix and contain PSA concentrations of

4, 10, 20, 50 and 108 ng/mL respectively. Levels 1, 2, 3, 4, and 5 are used to calibrate the FPSA assay.

VI.   Alternative Practices and Procedures

Transrectal ultrasonography (TRUS) of the prostate can provide additional information about prostate abnormalities and guide prostate biopsy. Digital rectal examination and total PSA results are alternative procedures used to aid in the detection of prostate cancer.

VII.   Marketing History

The Dimension® FPSA Flex® reagent cartridge for the Dimension® clinical chemistry system with heterogeneous immunoassay module has not been marketed commercially.

VIII.   Potential Adverse Effects of the Device on Public Health

Since low ratios of FPSA to total PSA can occur in patients with benign prostatic disorders and elevated ratios are not always associated with absence of disease, patient status must not be assessed entirely by FPSA or %FPSA results but in conjunction with information from a complete clinical evaluation including DRE or other diagnostic tests. Potential adverse effects are:

1.   A falsely elevated FPSA or %FPSA result (false negative) may lead to a delay beneficial treatment.
2.   A falsely low FPSA or %FPSA result (false positive) may cause unnecessary biopsy and needless therapy.

IX.   Summary of Pre-Clinical Studies

All pre-clinical studies were conducted at Dade Behring to assess the analytical performance of the assay except otherwise indicated.

1.   Characterization of the Antibodies

The Dade Behring Dimension® FPSA Flex® reagent cartridge uses two PSA-specific murine monoclonal antibodies – one as capture and the other as tag antibody. The tag antibody is the same as the one used in the Dimension® PSA method (P000021) and binds to both FPSA and PSA-ACT. The capture antibody is a new reagent which binds specifically to FPSA as demonstrated by immunoassays with FPSA and PSA-ACT.

2.   Characterization of the Antigen

The free PSA antigen used for production of the Master pool and Stock Standard (used to prepare the Calibrators) was purified from human seminal fluid. The reference standard for these antigen preparations is the WHO PSA Standard, 1st I S 1999 (96/668) which is identical to the Stanford Standard 1994 for FPSA.

3. Performance Characteristics

a) Imprecision Analysis

The imprecision studies were determined according to the NCCLS guideline EP5-A (Guideline for Evaluation of Precision Performance of Clinical Chemistry Devices) with 3 lots of the Dimension® FPSA Flex® reagent cartridge. Two lots were run on two Dimension® RxL analyzers and one on the Dimension® Xpand™ analyzer. Three serum pools, one plasma pool and three quality control materials containing FPSA concentrations spanning the assay range were tested in duplicates twice a day for twenty days. The percent coefficient of variation for the within-run precision ranged from 1.34% to 2.05% and for the total precision, the % CV was from 1.91 to 3.31%.

The between-laboratory reproducibility was evaluated in three separate laboratories. Five samples with FPSA values spanning the range of 0 to 12 ng/mL were tested. Each sample was run in quadruplicates for a total of ten runs per site using three kit lots. The % CV for within-assay (1% to 6%), run-to-run (<1.7%), day-to-day (0% to 5.9%) and total (1.4% to 7.2%) variation across sample-site-lot combinations were within the acceptable limits.

b) Lot-to-lot performance

Dimension® FPSA Flex® reagent cartridge lot-to-lot variability was determined by assaying 45 patient serum samples, 10 patient plasma samples and three levels of QC material with 3 validation lots of Flex® cartridges on a Dimension® RxL analyzer. Linear regression analysis was performed for each pair of reagent lots. Regression statistics showed slope values between 0.95 and 1.05, y-intercepts between -0.01 ng/mL and 0.02 ng/mL and correlation coefficients of 0.99 or greater.

c) Linearity

Linearity across the assay range was evaluated by testing five serial dilutions of the Dimension® T/F PSA Level 5 Calibrator (50 ng/mL) with one lot of Dimension® FPSA Flex® reagent cartridge on a Dimension® RxL analyzer. Concentrations of the samples ranged from 0 ng/mL to 50 ng/mL. Linear regression analysis of observed values versus calculated values yielded $y = 0.29$ ng/mL $+ 1.02x$ and $r = 0.999$. Results were also analyzed by quadratic regression ($y = 0.03$ ng/mL $+ 0.97x + 0.001x^2$, $r > 0.999$) and gave a p-value of 0.178. These results confirmed that the assay is linear across the assay range.

d) Recovery

Eleven serum samples were serially diluted across the assay range and the measured recovery was compared to the calculated recovery. For each sample, four dilutions were performed: 2:1, 1:1, 1:2 and 1:3. The average recovery for each sample was between 95% and 104% and the overall mean recovery was 99%.

e)   Analytical sensitivity

Analytical sensitivity was determined by testing Level 1 of the Dimension® T/F PSA Calibrator twenty consecutive times using three Dimension® FPSA Flex® reagent cartridge lots on both Dimension® RxL and Dimension® Xpand™ analyzers. The analytical sensitivity was ≤ 0.008 ng/mL and met the specified claim of 0.05 ng/mL.

f)   Functional Sensitivity

The functional sensitivity was determined by testing ten serum samples containing low concentrations of FPSA (0.004 ng/mL and 0.105 ng/mL). Each sample was run in replicates of 10 on a Dimension® RxL analyzer. For each sample, the mean FPSA concentration and the coefficient of variation (CV) were calculated. The CV was plotted as a function of analyte concentration and the FPSA concentration at which the CV was 20% was defined as the functional sensitivity. The overall functional sensitivity was within the acceptable limit of 0.03 ng/mL.

g)   High Dose Hook Effect

The objective of the high dose hook effect study was to determine if samples containing very high FPSA values might yield results less than the upper limit of the assay range. Seven serum samples with FPSA concentrations ranging from 5,000 ng/mL to 40,000 ng/mL were analyzed in replicates of five. The mA/min of each sample was compared to the mA/min of the Level 5 Dimension® T/P Calibrator. All samples from 5,000 ng/mL to 30,000 ng/mL were correctly reported. No high dose hook effect was observed for FPSA concentrations up to 30,000 ng/mL which met the specification of 10,000 ng/mL.

h)   Sample Carryover

A sample containing 50,000 ng/mL TPSA and 5,000 ng/mL FPSA was run alternately before and after a normal female serum as test and control respectively. The carryover result was 0.03 ng/mL, which was within the defined value of <0.1 ng/mL.

i)   Cross-reactivity

•   Prostatic Acid Phosphatase (PAP)

PAP cross-reactivity was assessed by spiking PAP into a normal female serum to a final concentration of 1,000 ng/mL. A control female serum was similarly spiked with phosphate buffered saline. Both samples were run in replicates of five on the Dimension® RxL analyzer with one validation lot of Dimension® FPSA Flex® reagent cartridge. The mean recovery for both samples was 0 ng/mL indicating PAP at a concentration of 1,000 ng/mL is below the detection limit of the assay.

•   PSA complexed to α1-Antichymotrypsin (PSA-ACT)

PSA-ACT used in this study was ≥99% purity for PSA-ACT and contained ≤1 ng/mL FPSA. The sample was diluted to a concentration of 100 ng/mL PSA-ACT and assayed in replicates of five on a Dimension® RxL analyzer with one Dimension® FPSA Flex® reagent lot. The measured FPSA in the PSA-ACT sample was 0.27 ng/mL and the control sample was 0.04 ng/mL. The difference was 0.23 ng/mL FPSA, and was no greater than the FPSA in the original PSA-ACT sample. These results demonstrated that PSA-ACT has no significant cross-reactivity.

j)   Interference

The effect of potentially interfering endogenous and exogenous substances were evaluated by either spiking the test substances into aliquots of a low FPSA serum pool or by mixing a high FPSA serum with a serum sample containing the test substance. None of the compounds tested (refer to listing in product labeling) interfered with assay performance at the concentrations given..

Interference due to human anti-mouse antibody (HAMA) was minimized by addition of polyclonal mouse IgG to the enzyme diluent and the chrome diluent. In addition, bovine IgG is added to the enzyme reagent to block other heterophile antibodies. To confirm that HAMA does not interfere with assay performance, 8 confirmed HAMA samples spiked with free PSA (1-2 ng/mL) were analyzed undiluted or treated with a nonspecific binding cocktail. The % recovery of all 8 samples were acceptable and within 5% of the control concentration.

k)   Reagent Stability

•   Open well stability

The Dimension® FPSA Flex® reagent cartridge contains three wells with substrate tablets and one well with chrome tablets. Once the tablets were hydrated, the well has a limited "open well stability". Open well stability for the substrate wells and the common wells was evaluated separately using 3 lots of Flex® reagent cartridges on Dimension® RxL and Xpand™ analyzers. Fresh Flex® reagent cartridges were included at each test point. Calibrator levels 1, 3 and 5 were assayed as test samples. Open well drift was ≤ 8% over a period of 15 days for the common wells and ≤ 4% over a period of 5 days for the substrate wells. These data substantiate the open well stability claims.

•   On-instrument stability

On-instrument stability is defined as the stability of unused/unopened cartridges stored refrigerated onboard of a Dimension® analyzer. A Flex® reagent cartridge was loaded on the analyzer and stored for 31 days. On day 31, a fresh cartridge from the same lot was loaded onto the instrument and Calibrators 1 to 5 were assayed with both cartridges. The differences in recovery between the fresh and the stored cartridges were within specification and therefore support the 30 days on-board stability claim.

l)   Stress testing at elevated temperatures and freeze/thaw conditions

The purpose of this study was to determine the impact of shipping conditions on the Dimension® FPSA Flex® reagent cartridge. Results showed that Flex® components were sensitive to storage at elevated temperatures. The daily drift at 25°C, is approximately 0.5%, at 35°C is 1.5% and at 45°C is >8%. Short exposure to elevated temperatures and few freeze/thaw cycles did not significantly affect the device performance and repeated freeze thaw cycles over seven days also did not appear to affect the assay.

m)   Dimension® FPSA Flex® reagent cartridge stability

In these experiments, three lots of FPSA Flex® reagent cartridges were stored between 2°C and 8°C and tested at specified intervals. Test results supported an expiration dating of 6 months.

n)   Calibration frequency

The objective of the study was to determine the frequency of calibration required. A single lot of calibrator was used to calibrate a Dimension® RxL analyzer. Five replicates of each calibrator were analyzed on day 0, 1, 2, 3, 4 and 7. Thereafter, each calibrator level was tested weekly over a period of 91 days. A least squares linear regression analysis was performed on the mean detected analyte value versus day of the study. The drift was calculated from the slope of the regression line using the intercept as the starting analyte concentration using the formula % drift = [(slope/intercept) x #days]*100. Results support the recommended 90-day calibration frequency.

o)   Equivalence of Dimension® RxL and Dimension® Xpand™ Systems

For this study, 76 samples (57 sera, 10 plasmas and 9 quality control samples) were assayed in duplicates with a single lot of FPSA Flex® reagent cartridge on a Dimension® RxL analyzer and a Dimension® Xpand™ instrument analyzer. Linear regression analysis for all samples showed a slope of 0.98, a y-intercept of 0.09 and a correlation coefficient of 0.999. Passing Bablock analysis showed a slope of 0.99 (95% CI: 0.979, 0.996), a y-intercept of 0.022 (95% CI: 0.006, 0.028) and a correlation coefficient of 1.000. Results support the equivalence performance of Dimension® RxL and Xpand™ instrument systems.

X.   Summary of Clinical Studies

1)   Clinical Study Objective

The primary objective of this clinical study was to determine the safety and effectiveness of the Dimension® FPSA device in men 50 years of age or older whose total PSA levels ranged between 4 and 10 ng/mL and have DRE results not suspicious for cancer to distinguish prostate cancer from benign prostatic conditions when used in conjunction with the Dimension® TPSA assay. To evaluate this, Receiver Operator Characteristic (ROC) curves were generated for %FPSA and for total PSA and the %FPSA cutoff was determined which

should detect 91% of the cancers in the cohort (sensitivity). The corresponding percent decrease in biopsies was then determined for this cutoff (specificity). The area under the ROC curve (AUC) for %FPSA and total PSA was compared to determine which method was a better discriminator between prostate cancer and benign conditions.

2)   Study Design

A multicenter clinical was conducted using prospectively collected samples from men who have been referred to an Urologist for determination of the presence of prostate cancer. The samples were accrued from 8 clinical sites in the United States. All samples were obtained under IRB approved protocols with patient informed consent. In addition, the study included samples from 416 healthy men 50 years of age or older who met the American Red Cross blood donation criteria and had no history of prostate disease. Six hundred and ninety-one samples were banked and analyzed by Diagnostic Oncology CRO.

3)   Subject Selection and Exclusion Criteria

Inclusion criteria for the disease cohort were as follows:

- All men aged 50 years or older regardless of race presented with symptoms to an urologist for evaluation of prostate cancer, including a transrectal prostate biopsy
- No history of treatment for benign prostate disease within 90 days prior to the referral
- No history of an evaluation for prostate cancer prior to the referral
- Had a DRE result that was not suspicious for cancer
- Have a total PSA value between 4 and 10 ng/mL as measured with the Dimension TPSA assay
- Can give a blood sample by venipuncture of at least 7 mL
- Can give a blood sample no more than 15 days prior to biopsy

Exclusion criteria

- Men younger than 50 years of age
- Men 50 years or older with a prior history of or treatment for prostate cancer
- Men 50 years or older with a history of benign prostatic disease who have been treated within 90 days of the referral
- Men who had undergone a DRE examination or other forms of prostate manipulation less than 5 days prior to the sample blood draw.

4)   Results

a)   Population Demographics

The median age of the disease cohort was 65.1 years. The ethnic composition of the study population consisted of 584 (84.5%) Caucasians, 84 (12.2%) African Americans, 8

(1.2%) Hispanic or Mexican, 7 (1%) Asian, 5 (0.7%) Native American and 3 (0.4%) Filipino men. Gleason scores were available for most subjects with 96% having scores of 7 or lower. The most frequent Gleason score was 6. The malignancy rate ranged from 24% to 35.9% with the overall rate of 29.5% which was similar to population malignancy rate of 30%. The mean total PSA value for the study cohort was 6.25 ±1.47 ng/mL.

b)   Biopsy result and cancer rate

The distribution of biopsy results in the disease cohort is given below.

Biopsy Result	# Subjects	% Total
Normal	160	23.2%
BPH	129	18.7%
PIN/Suspicious	198	28.7%
Prostate Cancer	203	29.4%
Total	690	100%

c)   Distribution of Total PSA, free PSA and % free PSA

The distribution of total PSA, free PSA and %FPSA by biopsy result is given below. Differences between benign and malignant groups were significant.

	Biopsy Result	Count	Mean	Median	Standard Error of Mean	p-value benign vs. malignant
Free PSA (ng/mL)	Benign	487	0.93	0.83	0.021	
	Malignant	204	0.75	0.66	0.029	
Total PSA (ng/mL)	Benign	487	6.11	5.7	0.074	0.145
	Malignant	204	6.60	6.5	0.108	
%FPSA	Benign	487	15.4	14	0.300	<0.001
	Malignant	204	11.5	10	0.420	

The distribution of total PSA, free PSA and %FPSA by biopsy result and age group is summarized in the following table. The mean values of %FPSA were significantly different between the age groups and between the biopsy results.

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	Age Group	Biopsy Result	Count	Mean	Median	Standard Error of Mean	p-value benign vs. malignant
Free PSA (ng/mL)	50-59	Benign	149	0.74	0.67	0.026	
		Malignant	52	0.56	0.53	0.034	
	60-69	Benign	194	0.91	0.82	0.031	
		Malignant	81	0.74	0.66	0.040	
	70+	Benign	144	1.15	1.00	0.047	
		Malignant	71	0.88	0.76	0.063	
Total PSA (ng/mL)	50-59	Benign	149	5.9	5.4	0.131	0.145
		Malignant	52	6.3	6.2	0.205	
	60-69	Benign	194	6.1	5.7	0.120	0.040
		Malignant	81	6.6	6.5	0.175	
	70+	Benign	144	6.3	6.1	0.132	0.014
		Malignant	71	6.9	6.8	0.183	
%FPSA	50-59	Benign	149	13.0	12	0.463	<0.001
		Malignant	52	9.1	8	0.565	
	60-69	Benign	194	15.0	14	0.437	<0.001
		Malignant	81	11.6	11	0.604	
	70+	Benign	144	18.2	18	0.604	<0.001
		Malignant	71	13.0	11	0.860	

d)   Positive predictive power of % FPSA at a single cut-off

Study results demonstrated that %FPSA enhanced the specificity of testing with total PSA for prostate cancer detection in men with PSA values between 4 and 10 ng/mL and DRE not suspicious of cancer. The table below shows the sensitivity and specificity estimates for the various %FPSA cut-offs. Using a single cut-off value of 19%, 91.2% (95%CI: 87.0%-94.7%) of the cancers would have been detected and 27.9% (95% CI: 23.8%-32.1%) of men with benign disease would have been spared biopsy.

Sensitivity and Specificity estimates for the various %FPSA cut-offs.

%FPSA	Sensitivity	95% CI	Specificity	95% CI
17%	87.2%	82.4 to 91.5	36.7%	32.5 to 41.2
18%	89.7%	85.3 to 93.5	32.4%	28.3 to 36.8
19%	91.2%	87.0 to 94.7	27.9%	23.8 to 32.1
21%	94.1%	90.5 to 96.9	19.5%	16.0 to 23.3
23%	95.1%	91.8 to 97.6	12.9%	10.0 to 16.2
25%	96.1%	93.0 to 98.3	9.4%	7.0 to 12.4
32%	99.5%	98.2 to 100%	0%	N/A

Based on the cancer prevalence of 29.5%, sensitivity of 91.2% and specificity of 27.9%, the estimated positive predictive value of %FPSA at the 19% cut-off was 34.3% which was significantly greater than the prevalence of disease. The estimated negative predictive value was 87.2%.

The AUC for %FPSA was 0.694 (95% CI: 0.65 to 0.738) and was significantly greater than AUC for total PSA (0.597; 95%CI: 0.553 to 0.642). Thus, confirming that %FPSA

was a better discriminator between prostate cancer and benign prostatic diseases in this cohort of subjects 50 years or older, with non-suspicious DRE results and total PSA in the range of 4 ng/mL to 10 ng/mL.

e)   Risk Assessment

Logistic regression analysis was used to determine the probability of finding prostate cancer on biopsy with age, total PSA, FPSA and %FPSA as predictors. Results demonstrated that age and %FPSA were statistically significant variables. The table below shows the expected probability of finding prostate cancer on biopsy for men 50 years or older with non-suspicious DRE results and PSA results between 4.0 and 10.0 ng/mL. Since age is a significant predictor, the results were stratified by age decade (50-59, 60-69 and >70). It should be noted that with each age decade the probability of cancer increases as %FPSA decreases.

Probability of detecting prostate cancer for men with non-suspicious DRE results and TPSA range 4.0 to 10.0 ng/m
(Parenthesis indicate Binomial 95% Confidence Interval)

%FPSA	Age Groups (years)		
	50-59	60-69	70+
≤10%	40.2% (33.1 – 50.9)	47.1% (37.3 – 58.2)	66% (52.1 – 79.1)
11%-19%	14.7% (9.1 – 23.5)	24.1% (17.9 – 32.0)	31.6% (23.4 – 41.9)
≥20%+	7.1% (1.8 – 33.8)	14.3% (7.3 – 27.2)	12.5% (6.8 – 22.4)
Prostate Cancer Prevalence (%)	25.9	29.5	32.7

XI.   Conclusions Drawn from the Studies

According to the clinical study results, the use of %FPSA as measured by the Dimension® FPSA assay can increase the specificity of Dimension® total PSA for prostate cancer detection in men with PSA values of 4 to 10 ng/mL and with DRE results not suspicious of cancer. The clinical benefit is a reduction of 27.8% unnecessary biopsies in men being evaluated for prostate cancer. In addition, a significant relationship was found between %FPSA and the relative risk of cancer in individual men. Lower %FPSA values indicate higher risk and older men were at higher risk than younger men. The calculated risk estimates based on %FPSA and patient age maybe used by physicians to recommend treatment options. These results support the sponsor's claim that the Dimension® FPSA Flex® reagent cartridge assay is safe and effective for use as stated in the indication.

Safety

The Dimension® FPSA Flex® reagent cartridge is not recommended to be the sole diagnostic tool to confirm the presence or absence of prostate cancer. PSA values should be used in conjunction with DRE and prostate biopsy is required for diagnosis of cancer.

As a diagnostic test, the Dimension® FPSA Flex® assay involves removal of blood for testing. Blood is routinely collected for prostate cancer diagnosis. The test, therefore, presents no additional safety hazard to the patient being tested.

Benefit/Risk

The risks associated with this device are:
- The risk associated with venipuncture, and
- The risk that misinterpretation of %FPSA would subject the patient to unnecessary biopsy or deprive the patient of a medical treatment

The benefit of the device is increased specificity when used to determine whether patients with total PSA between 4-10 ng/mL and DRE results not suspicious for cancer should be biopsied. With a 19% free PSA cut-off, 27.9% of men could be spared unnecessary biopsy and have a 91.2% of cancers correctly identified. As a consequence, fewer men would be subjected to unnecessary biopsies and possibly fewer medical complications such as infection, bleeding, urinary retention and hospitalization.

Borderline total PSA values (near 4 ng/mL), might suggest the need for increased follow-up. Similarly, patients who have a negative first biopsy with a %FPSA suggesting high risk might consider undergoing a second biopsy, since approximately 20% of cancers were reportedly missed on the first biopsy.

XII.   Panel Recommendations

Pursuant to Section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not the subject of an FDA Immunology Devices Advisory Panel meeting because the information in the PMA substantially duplicated information previously reviewed by this Panel.

XIII.   CDRH Action of the Application

The applicant's manufacturing facility was found to be in compliance with the Quality Systems Regulation (21 CFR 820). CDRH issued an approval order on January 24, 2003.

XIV.   Approval Specifications

Directions for Use: See labeling

Hazards to Health from Use of the Device: See Contraindications, Warnings, Precautions and Adverse Events in the attached labeling.

Postapproval Requirements and Restrictions: See approval order.