Summary of Safety and Effectiveness

I. General Information

Device Generic name(s):	Immunoassay for the *in vitro* quantitative determination of free prostate specific antigen (PSA) in human serum and plasma
Device Trade name(s):	Elecsys® Free PSA Immunoassay Elecsys® Free PSA CalSet Elecsys® Free PSA CalCheck
Applicant's name and address	Roche Diagnostics Corporation 9115 Hague Road Indianapolis, IN 46256 USA
PMA number:	P000027
Date of Panel recommendation:	None
Dates of Good Manufacturing Practice Inspection	January 25, 1999; September 30, 1999; and July 18, 2000
Date of notice of approval to the applicant	December 12, 2000

II. Intended Use/Indications for Use

Immunoassay for the *in vitro* quantitative determination of free prostate-specific antigen in human serum and plasma. The Elecsys free PSA immunoassay is indicated for measurement of fPSA in conjunction with the Elecsys total PSA assay to develop a ratio (%fPSA) of fPSA to tPSA. This ratio is useful when used in conjunction with the Elecsys Total PSA test as an aid in distinguishing prostate cancer from benign prostatic conditions in men age 50 years or older who have a rectal examination (DRE) that is not suspicious for prostate cancer and an Elecsys total PSA value in the range 4 ng/ml to 10 ng/ml. Prostate biopsy is required for diagnosis of prostate cancer. The electrochemiluminescence immunoassay "ECLIA" is intended for use on the Roche Elecsys 1010 and 2010 immunoassay analyzers.

III. Contraindications, Warnings and Precautions

There are no known contraindications for the Elecsys® free PSA Immunoassay.

Warnings and precautions are stated in the product labeling.

IV. Device Description

The Elecsys® Free PSA CalSet is used for calibrating the quantitative Elecsys Free PSA Immunoassay on the Elecsys 1010 and 2010 Immunoassay Analyzers. The Elecsys® Free PSA CalCheck is used for verifying the calibration of the Elecsys Free PSA Immunoassay on the Elecsys®1010 and 2010 Immunoassay Analyzers.

Kit Description - The kit contains three reagents: Streptavidin-coated microparticles, biotinylated Anti-PSA antibody, and ruthenium labeled Anti-PSA antibody which are combined in the "Reagent pack" (a bundle of three reagent bottles which is placed on the instrument as a single unit).

The Elecsys® Free PSA CalSet is a two-level calibrator intended for use in the calibration of the Elecsys® Free PSA Immunoassay on the Elecsys® 2010 and 1010 Immunoassay Analyzers.

The Elecsys® Free PSA CalCheck may be used for the verification of the calibration established by the Elecsys® Free PSA reagent and CalSet on the Elecsys® 2010 or 1010 Immunoassay Analyzers. This kit consists of three reagents, comprising three levels of Free PSA.

Test Principle - The Elecsys Free PSA immunoassay is a two monoclonal antibody sandwich assay that recognizes only free prostate-specific antigen not complexed with inhibitors such as α-1-anti-chymotrypsin. Free PSA in a sample, calibrator, or control bind with a biotinylated monoclonal free PSA-specific antibody and a monoclonal free PSA-specific antibody labeled with a ruthenium complex to form a sandwich complex. After incubation and the addition of streptavidin-coated microparticles, the complex binds with the solid phase via interaction of biotin in the sandwich complex and streptavidin coated particles. The reaction mixture is transferred to the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed by washing. Application of a voltage to the electrode induces chemiluminescent emission, which is measured by a photomultiplier. Free PSA Results are determined by instrument-specific calibration generated by 2-point calibration in conjunction with a master curve previously provided to the analyzer. The amount of emitted light from the calibrators and previously determined free PSA concentration of the calibrators form a standard curve to which samples and controls are compared. The

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concentration of samples and controls are automatically calculated by the analyzer and automatically reported for each specimen.

V. Alternative Practices and Procedures

Alternative practices and procedure for aiding in the detection of prostate cancer include transrectal ultrasonography (TRUS), digital rectal examinations and total PSA results. Patients with a suspicious digital rectal examination or total PSA values between 4.0 and 10 ng/mL may be referred for prostate biopsy.

VI. Prior Marketing History

The Elecsys Free PSA Immunoassay and Elecsys Free PSA CalSet have been marketed worldwide since August, 1997. The device has not been withdrawn in any country for reasons relating to the safety and effectiveness of the device. The Elecsys Free PSA CalCheck has not been marketed commercially.

VII. Potential Adverse Effects of the Device on Health

Since low ratios of free to total PSA occur in patients with benign prostatic disorders and elevated ratios are not always associated with absence of disease, assessment of patient status must not be based entirely on free PSA results. Potential adverse effects are: (1) a falsely low ratio could lead to a medical decision causing unnecessary biopsy and (2) a falsely elevated ratio could lead to a medical decision depriving the patient of potentially diagnostic biopsy results and subsequent treatment.

The concentration of free PSA in a given specimen determined with assays from different manufacturers can vary due to differences in assay methodology and reagent specificity. The results reported by the laboratory to the physician must include the identity of the free PSA assay used. Values obtained for both free and total PSA from different PSA assays cannot be used interchangeably. The Elecsys free PSA immunoassay should be used with the Elecsys total PSA immunoassays to calculate the ratio of free PSA to total PSA. Use of another manufacturer's total PSA assay may result in significantly different ratios, cutoffs, and cancer probabilities than represented in the Expected values. Ratios must be calculated using tPSA and fPSA results both obtained on the Elecsys 1010 innumoassay analyzer or both obtained on the Elecsys 2010 immunoassay analyzer.

Total PSA devices are not indicated as the sole diagnostic tool to confirm the presence or absence of malignant prostate disease. Patients with confirmed prostate cancer may have serum total PSA serum levels within the normal range. Some patients with non-malignant diseases of the prostate, including benign prostatic hyperplasia (BPH), may have elevated serum total PSA levels. Therefore, serum PSA values should be used in conjunction with the information from a complete clinical evaluation including DRE or other diagnostic tests. Confirmation of prostate cancer can only be determined by prostatic biopsy.

Manipulations of the prostate including DRE, needle biopsy and transurethral resection can cause transient and often large increases in serum free and total PSA levels. Therefore, blood samples for PSA measurement should be taken before performing these procedures. Additional blood testing should be delayed at least 2 weeks to allow serum PSA to return to original levels.

VIII. Summary of Non-Clinical Studies

In-house and external studies were conducted to assess the analytical performance characteristics of the Elecsys Free PSA Immunoassay.

Imprecision Analysis

The coefficients of variation for the sources of error in the Elecsys Free PSA Assay were determined with three lots of reagent, at three sites on both the Elecsys 1010 and 2010 Immunoassays Analyzers. The following tables of within run and total imprecision results for each Elecsys Immunoassay Analyzer represent the ranges of the coefficients of variation (%CV) in which the lot and site components have been combined.

Within Run Imprecision - Elecsys 1010

Sample	Free PSA, ng/mL	Median % CV
PreciControl TM 1	1.81	1.92
PreciControl TM2	13.61	2.23
Human Serum Pool 1	0.146	3.30
Human Serum Pool 2	2.28	3.02
Human Serum Pool 3	26.07	2.74

Total Run Imprecision - Elecsys 1010

Sample	Free PSA, n /mL	Median %CV
PreciControl TMl	1.81	6.06
PreciControl TM2	13.61	6.26
Human Serum Pool 1	0.146	7.04
Human Serum Pool 2	2.28	7.39
Human Serum Pool 3	26.07	7.83

Within Run Imprecision - Elecsys 2010

Sample	Free PSA, n /mL	Median %CV
PreciControl TMl	1.89	3.51
PreciControl TM2	14.04	3.71
Human Serum Pool 1	0.146	4.48
Human Serum Pool 2	2.44	4.31
Human Serum Pool 3	27.55	4.02

Total Imprecision - Elecsys 2010

Sample	Free PSA, ng/mL	Median %CV
PreciControl TMl	1.89	4.76
PreciControl TM2	14.04	4.55
Human Serum Pool 1	0.146	5.54
Human Serum Pool 2	2.44	5.56
Human Serum Pool 3	27.55	5.16

The median coefficients of variation for the Elecsys Free PSA Assay on the Elecsys 1010 (within run %CV of 3% and total %CV of 7%) and those on the Elecsys 2010 (within run %CV of 4% and total %CV of 5%) are representative of results obtained across multiple sites and multiple lots of reagent.

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Linearity Testing

Assay linearity was evaluated on both the Elecsys 2010 and the Elecsys 1010 by measuring dilutions created from five samples (concentration range from 0 to 40 ng/mL). Dilutions were evaluated using linear regression. The 95% confidence interval for the correlation coefficient was 0.9997 to 0.9999 on the Elecsys 2010 Immunoassay Analyzer and 0.9996 to 0.9999 on the Elecsys 1010 Immunoassay Analyzer. The slopes of the best fit line of observed concentration and expected concentration and the intercepts of the regression line for all samples were equivalent with theoretical values. These results indicate that assay results are linear with dilution within the range of 0 to 40 ng/ml.

Interference Testing

The effect of potentially interfering endogenous and exogenous substances on the Elecsys Free PSA Assay were evaluated on the Elecsys 2010 Immunoassay Analyzer. None of the compounds listed below interfered at the test concentrations given.

Potential Interferent	Test Concentration	Outcome ≤ ±10% limit
5'-Fluorouracil	1 mg/mL	Acceptable
Acetaminophen	0.2 mg/mL	Acceptable
Acetylsalicylic acid	0.5 mg/mL	Acceptable
Adriamycin / Doxorubicin-Hcl	0.1 mg/mL	Acceptable
Amethopterin-hydrate	4.5 mg/mL	Acceptable
Amikacin	0.15 mg/mL	Acceptable
Bilirubin	60 mg/dL	Acceptable
Caffeine	0.1 mg/mL	Acceptable
Cisplatin dichloride	20 mg/mL	Acceptable
Cortisol / hydrocortisone disodium salt	1 mg/mL	Acceptable
Cyclosporin A	2.97 ng/mL	Acceptable
Digoxin	5 ng/mL	Acceptable
Gentamycin sulfate	0.12 mg/mL	Acceptable
HAMA	1.66 mg/mL	Acceptable
Hemoglobin	500 mg/dL	Acceptable
Heparin	500 U/mL	Acceptable
Human serum albumin	120 mg/mL	Acceptable
Immunoglobulin G	30 mg/mL	Acceptable
Kanamycin monosulfate	0.15 mg/mL	Acceptable
Lidocaine HCl	0.06 mg/mL	Acceptable
Intralipid (lipemia)	1,000 mg/dL	Acceptable
Lithium carbonate	0.035mg/mL	Acceptable
Mitomycin C	0.06 mg/mL	Acceptable
PAP	1 µg/mL	Acceptable
Phenytoin sodium salt	0.1 mg/mL	Acceptable
Propanolol HCl	0.005 mg/mL	Acceptable
PSA (complexed)	231 ng/mL	Acceptable
Quinidine gluconate	0.05 mg/mL	Acceptable
Salicylic acid sodium salt	0.5 mg/mL	Acceptable
Streptomycin sulfate	0.15 mg/mL	Acceptable
Theophylline / Aminophylline	0.25 mg/mL	Acceptable
Tobramycin sulfate	0.0145 mg/mL	Acceptable
Valproic acid sodium salt	0.5 mg/mL	Acceptable

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Sample Stability Testing

Five samples were analyzed on an Elecsys 2010 Immunoassay Analyzer immediately and at subsequent times, temperatures of storage, and alternating cycles of freeze-thaw. Results of testing at various storage conditions and durations are listed in the table below.

Storage Condition	Duration
+ 20°C	3 days
+ 4°C	12 days
- 20°C	35 days
Freeze-thaw	5 cycles

Samples are stable at the conditions and times indicated in this table.

An additional sample stability study was performed in conjunction with this evaluation. A number of samples from normal and urologically-referred subjects were tested upon receipt, stored at -70°C and then assayed again approximately 95 to 110 days later. Free PSA results and the free PSA/total PSA ratios were within 10% of initial testing for the period of this study. These results indicate stability of free PSA values and free PSA/total PSA ratios when stored at –70°C.

Serum/Plasma Comparison

The free PSA concentrations of matched serum and plasma specimens from 46 subjects referred to a urologist and 50 normal subjects were compared to demonstrate the equivalency of sample matrices in the Elecsys Free PSA Assay. Studies were performed on the Elecsys 2010 and 1010 Immunoassay Analyzers. The results indicate that the following plasma sample collection systems are acceptable: sodium citrate (with correction for dilution as indicated in the package insert), potassium EDTA, sodium heparin, and lithium heparin

Limit of Detection

The smallest detectable concentration of free PSA was evaluated on the Elecsys 2010 and 1010 Immunoassay Analyzers. The limit of detection was defined as the concentration of free PSA corresponding to two standard deviations plus the mean value of the lowest calibrator (0 ng/mL). Twenty-one replicate determinations of free PSA were performed with the lowest master calibrator. The limit of detection of free PSA on the Elecsys 2010 and 1010 Immunoassay analyzer was less than 0.01 ng/ml.

Reagent stability on instrument analyzers

Reagent stability for a single reagent pack was determined on the Elecsys 2010 Immunoassay Analyzer with reagents stored at 22°C for up to 7 weeks. The acceptance criterion was ±10% of the initial value. Results support the recommendation of 6 weeks storage on the Elecsys 2010 Immunoassay Analyzer.

Reagent stability for a single reagent pack was determined on the Elecsys 1010 Immunoassay Analyzer with reagents stored at 23°C or alternately between 4°C and 23°C (2.5 hours at each test point) for up to 29 days. The acceptance criterion was ±10% of the initial value. The results support the recommendation of 4 weeks stability when alternating instrument and refrigerated storage.

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Calibration Stability

Calibration stability for a single reagent pack was evaluated on both the Elecsys 2010 and 1010 Immunoassay Analyzers by testing human serum pools and controls covering the assay range for an 8 day period. Results support 7 days of calibration stability for a single reagent pack stored on instrument.

Calibration stability for a single lot was evaluated by analyzing human serum pools and controls spanning the assay range over a 12 week period. Results support the calibration recommendation for a single lot.

High Dose Hook Effect

The upper limit from a high dose hook effect was evaluated on both analyzers by measuring dilutions of a sample having a high free PSA concentration before dilution (approximate initial concentration of 30,000 ng/mL). Results indicated that the limit for the high dose hook effect for the Elecsys Free PSA assay performed on the Elecsys 1010 and the Elecsys 2010 are greater than 30,896 and 33,380 ng/mL, respectively.

Comparison of analyzer results

The comparability of the Elecsys free and total PSA assays and the free/total PSA ratio performed on the 1010 and 2010 analyzer were evaluated by least squares linear regression analysis. Results were evaluated from 663 subjects utilized in the clinical studies who had total PSA results using the 2010 analyzer between 3.95 and 10.05 ng/ml and who had DRE results not suspicious for cancer. The results on the 2010 analyzer were utilized as the y-variable and the results on the 1010 as the x-variable. The results indicate a small analytical difference in free PSA result, total PSA result, and free/total PSA ratios between analyzers. The total difference between analyzers (fixed and proportional) for the free PSA assay was estimated to be 6% (2010 results higher than 1010 results). The total difference between analyzers for the total PSA assay was estimated to be 6% (2010 results lower than 1010 results). The total difference for the free/total PSA ratio was estimated to be 8% (2010 results higher than 1010 results). It is unclear if the analytical differences between analyzers leads to any significant difference in clinical interpretation of the free/total PSA ratios.

IX. Summary of Clinical Studies

Clinical Study Objective

The major objective of this premarket clinical study was to determine the safety and effectiveness of the device in men 50 years of age or older whose total PSA levels range 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 Elecsys Total PSA Immunoassay.**Study Design**

Multi-center studies were performed using 2 cohorts of males 50 years or older. A Normal healthy Cohort of 395 subjects collected under an IRB approved blood collection protocol with informed consent obtained serum samples from family practice physicians. For the Prospective Disease Cohort, 1602 samples were collected under an IRB approved protocol with patient informed consent from 39 community clinical practices or university related practices throughout the United States. These samples were obtained from men who had been referred to a urologist for determination of prostate cancer. Each site participated by collecting patient information and samples and shipping samples to a central testing laboratory. Data included demographics and clinical history. Samples were analyzed for total PSA using Elecsys Total PSA Immunoassay and Elecsys Free PSA Immunoassay at the testing laboratory. Of these 1602 samples, 1143 patients had DRE results that were not suspicious for cancer.

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Inclusion and Exclusion Criteria

The following inclusion and exclusion criteria were established for the prospective disease cohort:

Any male, regardless of race, presenting to a practicing urologist with symptoms that lead to an evaluation for prostate cancer, including a transrectal ultrasound guided prostate biopsy, was enrolled who:

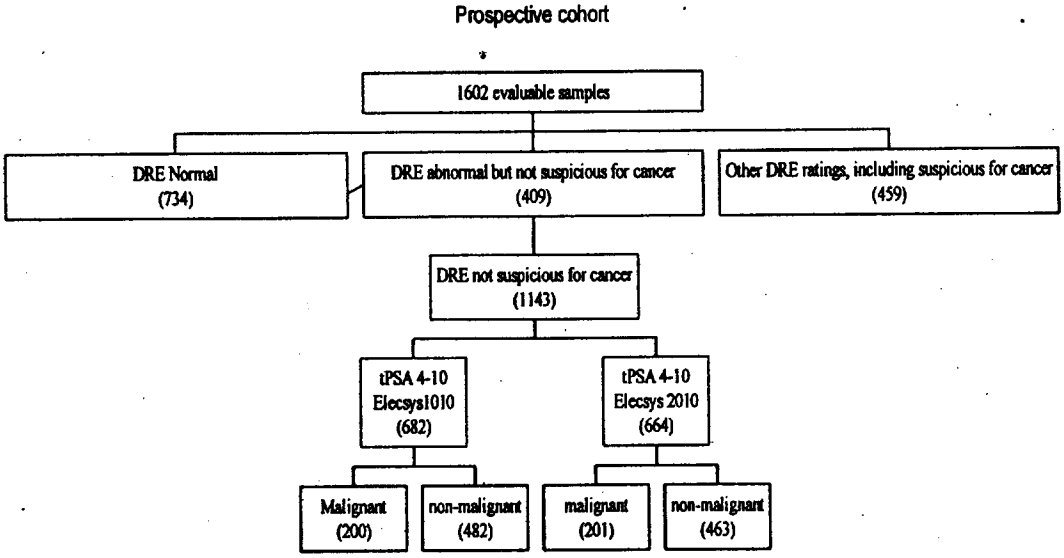
- Was age 50 or older
- Had not been treated for benign prostate disease within 90 days prior to the referral and was not taking any medications on the exclusion list.
- Had no history of an evaluation for prostate cancer prior to the referral.
- Had not had a DRE at least 5 days prior to blood sample
- Understood and signed the informed consent form
- Had medical records available for verification
- Gave a blood sample, by venipuncture, of at least 7 ml
- Gave a blood sample no more than 15 days prior to biopsy

Any male was excluded who:

- Was younger than 50 years of age
- Had a prior history of benign prostatic disease that had been treated within 90 days of the referral
- Had prior history of or treatment for prostate cancer
- Had undergone a DRE examination or other forms of Prostate manipulation less than 5 days prior to the blood sampling
- Failed to meet other inclusion criteria. Each subject could only be entered into the study once.

Results

Patients with PSA between 4 and 10 ng/mL and DRE Not Suspicious for Cancer were identified using each of the Elecsys immunoassay analyzers. A summary of the Prospective Sample Cohorts and Sub-cohorts evaluated in this study is shown in the following:



The number of patients in the cohorts for each analyzer was different. Samples with values very near the cut-off used as the selection criterion (3.95-10.05 ng/ml) were responsible for the difference.

Population Demographics

The median age of men with PSA between 4 and 10 ng/mL and a DRE Not Suspicious for Cancer was 66 years. Eighty-four percent (84%) of the men were Caucasian and 12% African American. Gleason Scores were available for most subjects. Ninety-six percent (96%) of the men had scores of 7 or less, with the most frequent score being 6. The cancer prevalence among all evaluable subjects was 0.343 ± 0.012. The cancer prevalence among subjects with total PSA between 4 and 10 ng/ml and DRE results not suspicious for cancer was 0.303 ± 0.018 using the Elecsys 2010 analyzer results and was 0.293 ± 0.017 using the Elecsys 1010 analyzer results.

Distribution of Biopsy Results

The distribution of biopsy results in these cohorts is given below. No significant differences were observed between the two analyzers.

Distribution of Biopsy Results

	Elecsys 1010		Elecsys 2010	
Biopsy Result	Subject count	Percent	Subject count	Percent
Normal	186	27.3	185	27.9
BPH	138	20.2	126	19.0
Prostatitis	117	17.2	112	16.9
PIN/Suspicious	41	6.0	40	6.0
Malignant	200	29.3	201	30.3
Total	682	100.0	664	100

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Distribution of Total PSA, Free, PSA, and Ratio of Free to Total PSA

The distribution of total PSA, free PSA, and ratio of free PSA to total PSA in these cohorts is given below. No clinically significant differences were observed between the two analyzers. Differences between benign and malignant groups were significant.

Elecsys1010 Immunoassay Analyzer PSA Statistics by Biopsy Outcome (Benign, Malignant)

	Biopsy Result	Count	Mean	Median	Standard Error of Mean	p-value benign vs. malignant
Free PSA	Benign	482	1.11	1.05	0.02	
	Malignant	400	0.96	0.87	0.03	
	Total	682	1.07	0.99	0.02	
Total PSA	Benign	482	6.18	5.87	0.07	p = 0.06
	Malignant	200	6.44	6.26	0.11	
	Total	682	6.26	5.98	0.06	
%fPSA/tPSA	Benign	482	18.22	17.3	0.30	p < 0.001
	Malignant	200	15.29	14.6	0.41	
	Total	682	17.36	16.8	0.25	

Elecsys 2010 Immunoassay Analyzer PSA Statistics by Biopsy Outcome (Benign, Malignant)

	Biopsy Result	Count	Mean	Median	Standard Error of Mean	p-value benign vs. malignant
Free PSA	Benign	463	1.19	1.11	0.02	
	Malignant	201	1.00	0.92	0.03	
	Total	664	1.13	1.06	0.02	
Total PSA	Benign	463	6.10	5.68	0.07	p = 0.02
	Malignant	201	6.42	6.10	0.11	
	Total	664	6.20	5.84	0.06	
%fPSA/tPSA	Benign	463	19.72	19.2	0.32	p < 0.001
	Malignant	201	16.00	15.2	0.42	
	Total	664	18.60	18.0	0.27	

Positive Predictive Power

The positive predictive power of a test is a function of the test's sensitivity and specificity. It is also a function of the prevalence of disease in the cohort on which the test is used. It can be shown that positive predictive power (P+) has the formula

$$P+ = \frac{P \times sen}{(P \times sen + (1 - P) \times fpr)}$$

Where

P = prevalence of disease
sen = sensitivity of the test at a particular cutoff
fpr = false positive rate of the test at a particular cutoff

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Positive Predictive Power (P+) for several cutoffs of %fPSA/tPSA are as follows:

	Elecsys 1010			Elecsys 2010		
Patients have %fPSA/tPSA below	Positive Predictive Power	% Cancers Correctly Identified	% Non-Cancers Correctly Identified	Positive Predictive Power	% Cancers Correctly Identified	% Non-Cancers Correctly Identified
10	51.9%	17.7%	93.3%	57.3%	11.9%	96.3%
15	39.1%	49.5%	68.5%	3.5%	43.5%	76.0%
20	33.4%	76.8%	37.6%	37.1%	71.5%	48.5%
25	31.1%	93.9%	15.2%	32.9%	92.2%	20.3%
30	30.1%	98.5%	6.5%	31.5%	99.0%	8.7%

Individual Risk Assessment

Percent free PSA has the potential use for determining the relative risk of prostate cancer in individual men. The table below shows the probability of detecting prostate cancer with needle biopsy in a urologically referred cohort of men fifty years of age or older, with rectal examination results that are not suspicious for cancer (1,143 men).

The information in the table below indicates that there is an increased risk of cancer detection as the PSA level increases. In a urologically referred cohort there is a 12% to 22% risk of cancer in men whose total PSA is less than 4.0 ng/ml. The risk of cancer in men who's total PSA is between 4 and 10 ng/ml is 26% to 33%. The PSA range of 4-10 ng/ml has been described in the literature as the diagnostic "gray zone." It is in this area that the percent free-PSA to total-PSA ratio is of utility.

Probability of Detecting Cancer with Needle Biopsy in Urologically Referred Men with Rectal Examination Results Not Suspicious for Cancer

	Elecsys 1010		Elecsys 2010	
Total PSA Range ng/ml	Probability of Cancer (%)	95% Confidence Interval	Probability of Cancer (%)	95% Confidence Interval
<4.0	15.7	10.9-20.6	17.1	12.4-21.6
4.0-10.0	29.3	25.9-32.7	30.3	26.8-33.8
>10.0	48.8	42.5-55.0	49.1	42.5-55.7

Probability of Cancer in the "Gray Zone"

The table below shows the expected probability of finding prostate cancer on needle biopsy for the cohort of men 50 years of age or older with a total PSA value between 4 and 10 ng/ml and digital rectal examination findings not suspicious for cancer. Since age is a factor in the development of cancer, the table is stratified by age decade (50-59, 60-69, >70). The estimates are derived from a loglinear model analysis of free to total PSA ratio in 4 categories (as noted in the table below) and age vs. cancer outcome.

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Probability of finding Cancer on Needle Biopsy by Age decade and fPSA/tPSA ratio

	Age groups					
	Elecsys 1010			Elecsys 2010		
fPSA/tPSA ratio	50-59	60-69	70+	50-59	60-69	70+
<=0.10	41.9%	51.1%	58.1%	48.4%	54.4%	61.9%
0.11 –0.18	22.7%	29.9%	36.1%	27.6%	32.6%	39.8%
0.19 – 0.25	16.6%	22.4%	27.7%	19.1%	23.0%	29.0%
>0.25	10.4%	14.4%	18.3%	9.8%	12.1%	15.8%

Note that the probability of cancer increases as the free/total PSA ratio decreases for each age decade. Note also that the cancer probability for the Elecsys 1010 is slightly different from the probability for the Elecsys 2010 at similar age decades and free/total PSA ratios but the differences appear minimal.

The table below shows the probability of finding prostate cancer on needle biopsy for the cohort of men 50 years of age or older with a total PSA value between 4 and 10 ng/ml and rectal examination findings not suspicious for cancer without loglinear modeling for age or free/total PSA ratio.

Unmodeled Probability of finding Cancer on Needle Biopsy By fPSA/tPSA ratio

fPSA/tPSA ratio	Elecsys 1010	Elecsys 2010
< 0.10	0.545 ± 0.057	0.593 ± 0.067
0.1 – 0.15	0.320 ± 0.033	0.371 ± 0.037
0.15 – 0.2	0.250 ± 0.031	0.304 ± 0.035
0.2 – 0.25	0.250 ± 0.038	0.228 ± 0.032
> 0.25	0.154 ± 0.041	0.144 ± 0.036
All	0.293 ± 0.017	0.303 ± 0.018

X. Benefit/Risk Analysis

The risks associated with this device are:

- The risk associated with venipuncture, and
- The risk that interpretation of a free PSA/total PSA ratio would subject the patient to unnecessary biopsy or deprive the patient of a medical treatment.

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The benefit of the device is the increased specificity offered by the use of the free PSA/total PSA ratio when used to determine whether patients with total PSA between 4-10 ng/mL and DRE results not suspicious for cancer should receive biopsies. With a 0.25 free/total PSA ratio cutoff, 15% to 20% of men could be spared unnecessary biopsy and have 92% to 95% of cancers correctly identified. As a consequence, fewer men would be given unnecessary biopsies as well as possible medical complications (infection, bleeding, urinary retention, and hospitalization).

There is a substantial risk of an unnecessary biopsy (~80%) for men without cancer when total PSA is between 4 and 10 ng/ml and DRE results not suspicious for cancer.

XI. Panel Recommendation

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Immunology Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel

XII. CDRH Decision on Application

FDA issued an approval order on December 12, 2000

The applicant's manufacturing facility was inspected on January 25 and September 30, 1999, and July 18, 2000, and was found to be in compliance with the Good Manufacturing Practice (GMP) regulation.

XIII. Approval Specifications

Directions for use: See the labeling.

Conditions of Approval: CDRH Approval of this PMA is subject to full compliance with the conditions described in the Approval Order.

Postapproval Requirements and Restrictions: See Approval Order.