



# Physician Instructions:

## PROGENSA® PCA3 Assay

### The First Molecular Test, Specific for Prostate Cancer, from Urine

#### OVERVIEW

Prostate cancer (PCa) is the most common cancer and the second leading cause of cancer death among men in the United States (American Cancer Society, 2011). Current practices for detecting PCa utilize serum PSA and DRE as indications for biopsy and approximately 25% of patients with elevated serum PSA are found to have PCa (Catalona, 1994; Schröder, 2009). This means that 75% of first biopsies are negative. The fear that cancer was missed often leads to repeat biopsies—most of which will also be negative—because there is not enough clear information provided by serum PSA and DRE to decide whether to proceed with or delay an additional biopsy. Men with one or more previous negative biopsies present a clinical dilemma and there is a medical need for additional tests to help physicians and patients make more informed repeat biopsy decisions.

PCA3 is a prostate-specific gene that is highly over-expressed in 95% of prostate cancers. Prostate cancer cells express 60 to 100 times more PCA3 RNA than normal cells (Hessels, 2003). The PROGENSA PCA3 Assay is highly specific and uses Transcription Mediated Amplification (TMA) to quantify PCA3 RNA in a patient sample.

The PROGENSA PCA3 Assay is the first FDA-approved urine-based molecular test that detects the over-expression of the PCA3 gene. The specific information provided by the test—the PCA3 Score—can be used in conjunction with other patient history to decide whether a repeat biopsy is necessary in men with one or more previous negative biopsies. Data on the PCA3 marker has been cited in over 100 publications (Salagierski, 2012) and more than 200,000 tests have been used in clinical practice throughout the world.

**PROGENSA PCA3 Assay—the test for better biopsy decisions.**

## ▶ INTENDED USE

The PROGENSA PCA3 Assay is an *in vitro* nucleic acid amplification test. The assay measures the concentration of prostate cancer gene 3 (PCA3) and prostate-specific antigen (PSA) RNA molecules and calculates the ratio of PCA3 RNA molecules to PSA RNA molecules (PCA3 Score) in post-digital rectal exam (DRE) first-catch male urine specimens. The PROGENSA PCA3 Assay is indicated for use in conjunction with other patient information to aid in the decision for repeat biopsy in men 50 years of age or older who have had one or more previous negative prostate biopsies and for whom a repeat biopsy would be recommended by a urologist based on current standard of care, before consideration of PROGENSA PCA3 Assay results.

A PCA3 Score <25 is associated with a decreased likelihood of a positive biopsy. Prostatic biopsy is required for diagnosis of cancer.

### WARNINGS:

**The PROGENSA PCA3 Assay should not be used for men with atypical small acinar proliferation (ASAP) on their most recent biopsy. Men with ASAP on their most recent biopsy should be treated in accordance with current medical guidelines.**

**The Clinical Study only included men who were recommended by urologists for repeat biopsy. Therefore, the performance of the PROGENSA PCA3 Assay has not been established in men for whom a repeat biopsy was not already recommended.**

## ▶ LIMITATIONS OF CLINICAL STUDY RESULTS

- The PCA3 Score is intended to be used in conjunction with serum prostate-specific antigen (PSA) and other risk indicators to guide appropriate patient management in the “at risk” population of men who have had one or more previous negative prostate biopsies and for whom a repeat biopsy would be recommended based on current standard of care.
- Performance of the PROGENSA PCA3 Assay has not been established in men who undergo repeat biopsy less than three months or more than seven years after their most recent negative biopsy.
- The effect of medications known to affect serum PSA levels such as finasteride (Proscar, Propecia), dutasteride (Avodart) and anti-androgen therapy (Lupron) on PROGENSA PCA3 Assay performance was not evaluated.
- Certain therapeutic and diagnostic procedures, such as prostatectomy, radiation, prostate biopsy and

others, may affect the viability of prostatic tissue and subsequently impact the PCA3 Score. The effect of these procedures on assay performance has not yet been evaluated. Samples for PROGENSA PCA3 Assay testing should be collected when the clinician believes prostate tissue has recovered.

- Results from the PROGENSA PCA3 Assay should be interpreted in conjunction with other laboratory and clinical data available to the clinician and relevant guidelines in the decision for repeat biopsy.

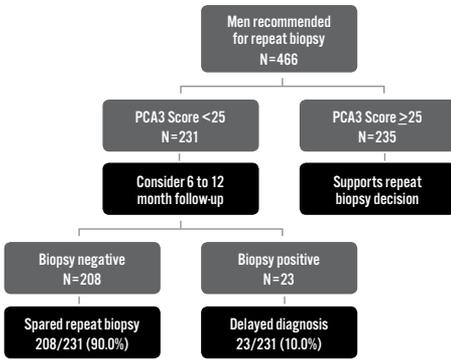
## ▶ CLINICAL SENSITIVITY AND SPECIFICITY OF THE PROGENSA PCA3 ASSAY

A pivotal, prospective, multicenter clinical study was conducted to evaluate the performance of the PROGENSA PCA3 Assay for assessing the likelihood of repeat biopsy outcome. In order to evaluate the clinical performance of PROGENSA PCA3 Assay, the clinical study data were analyzed to determine how the use of the PCA3 Score might have affected the repeat biopsy recommendation for the clinical study subjects.

The flow chart below summarizes the results of this analysis. In the clinical study of 466 subjects, 49.6% (231 out of 466) of subjects had PCA3 Scores <25. This indicates decreased likelihood of a positive repeat biopsy result, so the clinician and patient might have considered delaying the repeat biopsy. Of these 231 men, 208 (90%) subsequently had a negative biopsy result, while 23 (10%) had a biopsy positive for prostate cancer. For the 235 men with PCA3 Scores ≥25, the PROGENSA PCA3 Assay result supports the decision to repeat biopsy (34% (79/235) of these men had positive biopsies).

The potential clinical benefit is that 44.6% (208 out of 466) of men in the study may have been spared an unnecessary repeat biopsy. Instead, these men would have been monitored closely for any change in risk factors that would suggest disease. The associated risk is that 23 of the men who had a biopsy positive for prostate cancer may have had their diagnosis delayed. The standard timeframe for conducting follow up with the intended use population is six to twelve months. In terms of risk versus benefit, nine men may have avoided an unnecessary repeat biopsy for every one man whose diagnosis may be delayed. In the context of the entire study population (466 total subjects), 49.6% (231/466) of prostate biopsies would have been avoided and 4.9% (23/466) of men who harbored biopsy-detectable prostate cancer would have been monitored instead of receiving an immediate repeat biopsy. The PROGENSA PCA3 Assay should not be used for men with atypical small acinar proliferation (ASAP) on their most recent biopsy. Men with ASAP on their most recent biopsy should be treated in accordance with current medical guidelines.

## ► SUMMARY OF CLINICAL STUDY RESULTS



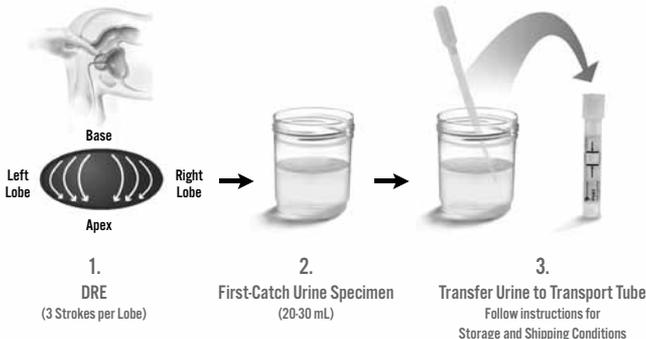
## ► INSTRUCTIONS FOR URINE SPECIMEN COLLECTION AND PROCESSING

1. Conduct a DRE as depicted above immediately prior to urine collection: Apply pressure on the prostate, enough to depress the surface, from the base to the apex and from the lateral to the median line for each lobe and repeat this three times.
2. Following the DRE, direct the patient to provide first-catch urine (approximately 20 to 30 mL of the initial urine stream) in an appropriately labeled urine collection cup. This must be the first voided urine specimen following the DRE. Use a collection cup free of any preservatives. If a patient cannot stop his urine flow and provides more urine than the requested first 20 to 30 mL, keep the entire volume. Very high urine volumes can lower PCA3 and PSA analyte concentrations and may infrequently result in an invalid specimen. Thus, the patient should try to

avoid filling the urine collection cup. If the patient is unable to provide the requested volume of urine (at least 2.5 mL is required to run the PROGENSA Assay) then the specimen must be rejected.

3. Unprocessed urine specimens, if not immediately processed, must be maintained at 2°C to 8°C or kept on ice. The chilled, unprocessed urine specimen must be transferred into the urine specimen transport tube within four hours of collection. Otherwise, the specimen must be rejected and the urologist must collect a new specimen. Do not freeze unprocessed urine specimens.
4. To process urine specimens, tightly cap and invert the urine specimen five times to resuspend cells. Remove the cap of the urine specimen transport tube and transfer 2.5 mL of the collected urine into the tube using the disposable transfer pipette provided. The correct volume of urine has been added when the fluid level is between the black fill lines on the urine specimen transport tube label.
5. Re-cap the urine specimen transport tube tightly and invert the urine specimen five times to mix. This is now known as the processed urine specimen.
6. Processed urine specimens must be transported to the laboratory in the urine specimen transport tube. Processed samples may be shipped under ambient conditions (without temperature control) or frozen—please ship or transport processed urine specimens according to instructions provided by your testing laboratory. Shipping arrangements must be made to ensure specimens are received by the testing site within five days of collection. If a sample is shipped under ambient conditions and is received by the testing laboratory more than five days after specimen collection, the specimen must be rejected.

### The PCA3 Urine Specimen Collection Procedure



## ► INTERPRETATIONS OF RESULTS

The PCA3 Score is calculated as the ratio of PCA3 RNA copies to PSA RNA copies, multiplied by 1000. As the PCA3 Score increases, the likelihood for a positive biopsy increases. As the PCA3 Score decreases, the likelihood for a positive biopsy decreases.

If the reported PCA3 Score is below the cut-off of 25, the result should be interpreted as NEGATIVE. If the PCA3 Score is above or equal to the cut-off of 25, the result should be interpreted as POSITIVE. A NEGATIVE result is associated with decreased likelihood of a positive biopsy.

Due to normal assay variability, specimens with PCA3 Scores near the cutoff of 25 (i.e., 18 to 31) could yield a different overall interpretation of POSITIVE or NEGATIVE upon repeat testing. PCA3 Scores in the range from 18 to 31 should therefore be interpreted with caution. The PCA3 Score should be used in conjunction with other patient information to aid in the decision for repeat biopsy.

Sometimes a <[Calculated Score] or >[Calculated Score] is reported. This occurs if the PCA3 and/or PSA analyte concentration is outside the quantitative range. If <[Calculated Score] is below the cut-off of 25, the result should be interpreted as NEGATIVE. If >[Calculated Score] is above the cut-off of 25, the result should be interpreted as POSITIVE. In some cases, it may not be possible to determine if a specimen is POSITIVE or NEGATIVE. If the PCA3 Score is indeterminate relative to the cutoff of 25, another specimen must be collected from the patient and retested.

The laboratory may request an additional urine specimen if the laboratory cannot provide a PCA3 Score which can be used for interpretation relative to the cutoff of 25.

For more detailed information about PROGENSA PCA3 Assay, please visit [www.gen-probe.com/inserts](http://www.gen-probe.com/inserts) at [www.gen-probe.com](http://www.gen-probe.com).

References available at [www.gen-probe.com](http://www.gen-probe.com). PROGENSA and GEN-PROBE are trademarks of Gen-Probe Incorporated.

