

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

K050063

B. Purpose for Submission:

New submission

C. Measurand:

P63 protein

D. Type of Test:

Immunohistochemistry reagent

E. Applicant:

Asymmetrx Inc.

F. Proprietary and Established Names:

Trade/Proprietary Name: Prostate-63 Cancer Diagnostic Test

Common Name: Anti-p63 Prostatic basal cell antibody

G. Regulatory Information:

1. Regulation section:

21 CFR 864.1860, Immunohistochemistry reagents and kits

2. Classification:

Class I. Device exceeded the limitations to 21 CFR 864.9 (limitations to exemption from premarket notification) since a new indication for use that differed from other reagents or kits of this generic type (such as immunohistochemical anti-cytokeratin antibodies) was utilized.

3. Product code:

NTR, Immunohistochemical reagent, antibody (monoclonal or polyclonal) to p63 protein in nucleus of prostatic basal cells

4. Panel:

Pathology (88)

H. Intended Use:

1. Intended use(s):

For In Vitro Diagnostic Use. The Prostate-63 Cancer Diagnostic Test features a mouse monoclonal antibody, clone 4A4, that recognizes the human p63 protein in the nucleus of prostatic basal cells and urothelial tissues. This test is intended for laboratory use to qualitatively identify by immunohistochemistry the p63 antigen in histological sections from formalin-fixed paraffin-embedded tissue of normal and/or pathological prostate tissue obtained by needle biopsy or surgical procedures. The presence or absence of p63 staining aids the pathologist in the differential diagnosis of prostate cancer in conjunction with morphological findings seen with hematoxylin and eosin staining complemented by proper

- controls. The clinical interpretation of any staining or its absence should be evaluated within the context of the patient's clinical history and other diagnostic tests by a qualified pathologist.
2. Indication(s) for use:
This test is intended for laboratory use to qualitatively identify by immunohistochemistry the p63 antigen in histological sections from formalin-fixed paraffin-embedded tissue of normal and/or pathological prostate tissue obtained by needle biopsy or surgical procedures. The presence or absence of p63 staining aids the pathologist in the differential diagnosis of prostate cancer in conjunction with morphological findings seen with hematoxylin and eosin staining complemented by proper controls. The clinical interpretation of any staining or its absence should be evaluated within the context of the patient's clinical history and other diagnostic tests by a qualified pathologist.
 3. Special conditions for use statement(s):
In Vitro diagnostic Use
 4. Special instrument requirements:
None

I. Device Description:

The reagent is described in 2 configurations: reagent only or reagent with a buffer for antigen retrieval methods. The antibody is provided in concentrated form within an appropriate buffer. Other general reagents and equipment commonly used in immunohistochemical staining methods are required but not supplied with the antibody reagent.

J. Substantial Equivalence Information:

1. Predicate device name(s):
There currently is no similar device currently cleared by premarket notification, therefore there is no legally marketed predicate device.
2. Predicate 510(k) number(s):
None
3. Comparison with predicate:
The device is similar to the general analytical methods of other immunohistochemical reagents but is used to assist the pathologist in the diagnosis of prostate cancer rather than aiding the determination of tissue type of cancerous or normal cells.

Similarities		
Item	Device	Predicate

Differences		
Item	Device	Predicate

K. Standard/Guidance Document Referenced (if applicable):

None referenced.

L. Test Principle:

The anti-p63 monoclonal antibody (clone 4A4) detects p63 protein by Immunohistochemical staining of formalin-fixed paraffin-embedded tissue obtained by needle biopsy or surgical procedures by standard immunocytochemical procedures. Antibody binding to portions of a tissue section is detected by using an anti-mouse IgG secondary antibody conjugated to horseradish peroxidase (HRP), which in turn enzymatically converts a chromogenic substrate to a visible reaction product to reveal prostatic basal cells. The specimen may then be counterstained and coverslipped. Results are analyzed by a qualified pathologist using light microscopy. The p63 protein is highly expressed in prostatic basal cells. These cells are typically absent in prostate carcinoma. The pattern of staining, or its absence, in appropriate cell structures and locations in a histological section assists in the diagnosis of prostate cancer.

M. Performance Characteristics (if/when applicable):**1. Analytical performance:****a. *Precision/Reproducibility:***

No specific precision data was provided since no common set of reagents is included in the device and laboratory use will employ other reagents, equipment, and biological stains common to many clinical histology laboratories. Use characteristics and performance will vary according to the conditions used in a particular laboratory.

b. *Linearity/assay reportable range:*

Not applicable

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

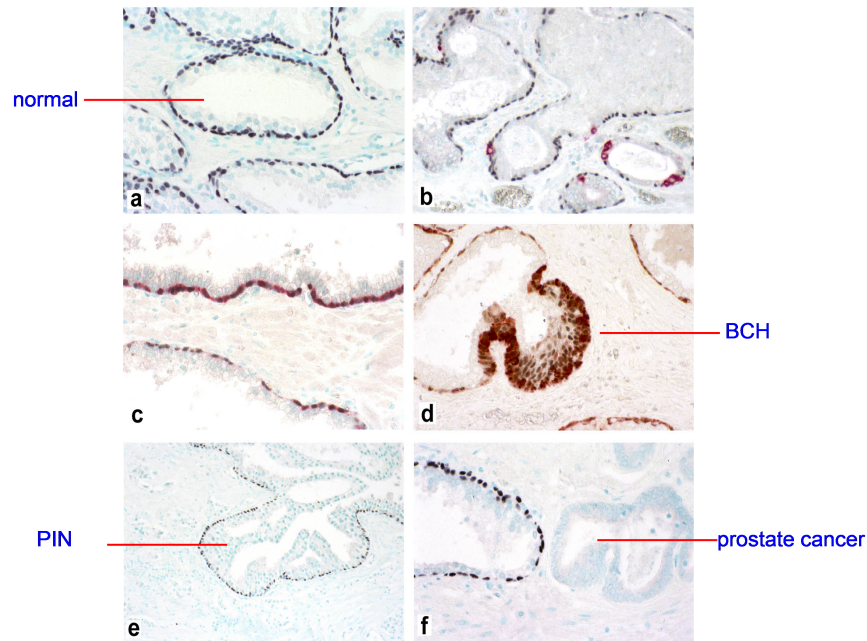
Not applicable

d. *Detection limit:*

Not applicable

e. *Analytical specificity:*

A typical staining pattern in both normal and prostate cancer tissue, sectioned and stained with the antibody reagent, is shown in the following figure.



f. *Assay cut-off:*

Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

Not performed

b. *Matrix comparison:*

Not Applicable

3. Clinical studies:

The labeling notes the following information and scientific literature :

The 4A4 anti-p63 monoclonal antibody recognizes all forms of p63 protein on western blots, and shows strong nuclear staining of baby hamster kidney (BHK) cells expressing p63 cDNAs but not BHK cells expressing control vectors (Yang et al., 1998). By immunohistochemistry in mouse tissues, the 4A4 anti-p63 monoclonal antibody recognizes basal cells of skin, breast, prostate, urothelia, among other tissues, but does not show significant staining in corresponding tissues of embryos lacking the p63 gene (Yang et al., 1999)

p63 stains prostatic basal cells of normal glands in needle biopsies with a sensitivity approaching 100% (Wu et al., 2004). Benign glands were also positive in 11 of 12 (95%) sections derived from transurethral resection of the prostate (TURP; Shah et al., 2002). p63 does not stain neuroendocrine or luminal, secretory cells of the prostate (Signoretti et al., 2000). As basal cells are absent from invasive prostate carcinoma (Hedrick and Epstein, 1989), p63 staining aids in the diagnosis of prostate carcinoma in biopsy sections. In one

study, p63-positive cells were absent in 126 of 130 (97%) needle biopsy specimens of invasive prostate cancers (Signoretti et al., 2000). In the remaining four cases, p63-positive signal was detected but in less than 1% of cells. In a similar study of needle biopsies, p63 staining was absent in 67 of 67 (100%) cases of prostate cancer (Shah et al., 2002). Despite the high sensitivity and specificity of the 4A4 anti-p63 antibody, not all glands stain uniformly with basal cell markers and some conditions that mimic prostate carcinoma display reduced or absent basal cell markers (Epstein, 2004). Therefore, failure to demonstrate p63-positive basal cells in any particular prostatic gland or group of glands may not be conclusive for malignant infiltration. Pathologists should interpret basal cell absence in the context of all histologic and cytologic features. When doubt remains, recutting the tissue block for deeper tissue levels is recommended.

Literature cited:

1. Epstein JI. Diagnosis and reporting of limited adenocarcinoma of the prostate on needle biopsy. *Mod Pathol*. 2004 Mar; 17(3):307-15.
2. Hedrick L, Epstein JI. Use of keratin 903 as an adjunct in the diagnosis of prostate carcinoma. *Am J Surg Pathol*. 1989 May; 13(5):389-96.
3. Shah RB, Zhou M, LeBlanc M, Snyder M, Rubin MA. Comparison of the basal cell-specific markers, 34betaE12 and p63, in the diagnosis of prostate cancer. *Am J Surg Pathol*. 2002 Sep;26(9):1161-8.
4. Signoretti S, Waltregny D, Dilks J, Isaac B, Lin D, Garraway L, Yang A, Montironi R, McKeon F, Loda M. p63 is a prostate basal cell marker and is required for prostate development. *Am J Pathol*. 2000 Dec;157(6):1769-75.
5. Yang A, Kaghad M, Wang Y, Gillett E, Fleming MD, Dotsch V, Andrews NC, Caput D, McKeon F. p63, a p53 homolog at 3q27-29, encodes multiple products with transactivating, death-inducing, and dominant-negative activities. *Mol Cell*. 1998 Sep;2(3):305-16.
6. Yang A, Schweitzer R, Sun D, Kaghad M, Walker N, Bronson RT, Tabin C, Sharpe A, Caput D, Crum C, McKeon F. p63 is essential for regenerative proliferation in limb, craniofacial and epithelial development. *Nature*. 1999 Apr 22;398(6729):714-8.
 - a. *Clinical Sensitivity:*
Not applicable
 - b. *Clinical specificity:*
Not applicable
 - c. Other clinical supportive data (when a. and b. are not applicable):
Not applicable
4. Clinical cut-off:
Not applicable
5. Expected values/Reference range:
See Figure above.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.