CONFIRM anti-Prostate Specific Antigen (PSA) Rabbit Polyclonal Primary Antibody

REF 760-2506

05266939001

IVD Σ 50

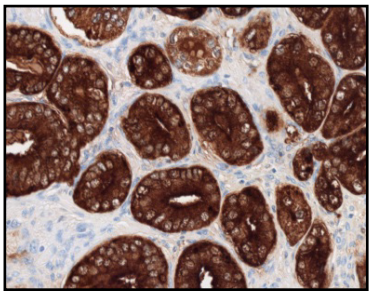

Figure 1. CONFIRM anti-PSA antibody staining on prostate carcinoma.

INTENDED USE

CONFIRM anti-Prostate Specific Antigen (PSA) Rabbit Polyclonal Primary Antibody is intended for laboratory use in the qualitative immunohistochemical detection of PSA by light microscopy in sections of formalin-fixed, paraffin-embedded tissue stained on a BenchMark IHC/ISH instrument.

This product should be interpreted by a qualified pathologist in conjunction with histological examination, relevant clinical information, and proper controls

This antibody is intended for in vitro diagnostic (IVD) use.

SUMMARY AND EXPLANATION

CONFIRM anti-Prostate Specific Antigen (PSA) Rabbit Polyclonal Primary Antibody (CONFIRM anti-PSA antibody) is a polyclonal antibody produced against the human PSA protein. PSA is a 34 kDa chymotrypsin-like serine protease that functions to liquefy the seminal fluid coagulum, thus helping in the release of spermatozoa.[1] In addition to being expressed in normal prostate epithelium, hyperplastic and malignant prostate tissues also express PSA.[1]

For metastatic tumors that do not readily present with a clinically known or suspected primary site, a series of organ or lineage-specific IHC studies may be used to aid in determining origin.[2] In this context, detection of PSA by IHC is widely used by pathologists to determine prostatic origin.[1,2,3] PSA positive IHC staining is observed in high percentages of lymph node metastases and distant metastases of prostate cancer samples.[4,5] PSA is also the only biomarker recommended by the European Society for Medical Oncology (ESMO) guidelines to show prostatic origin of a metastatic lesion.[6] Thus, IHC detection of PSA with CONFIRM anti-PSA antibody may be used as an aid in the identification of adenocarcinoma of the prostate in metastatic sites.

PSA is considered an established IHC marker to aid in distinguishing between prostate carcinoma (PSA+) and urothelial carcinoma (PSA-). This association is based on numerous studies that demonstrate PSA to be highly sensitive and specific for prostate carcinoma versus urothelial carcinoma.[3,7,8,9,10] Thus, IHC detection of PSA with CONFIRM anti-PSA antibody may be used to aid in the differentiation of prostate adenocarcinoma from urothelial carcinoma.

The staining pattern for this antibody is cytoplasmic. It may be used as part of a panel of IHC studies.

PRINCIPLE OF THE PROCEDURE

CONFIRM anti-PSA antibody binds to free and bound human PSA in formalin-fixed, paraffin-embedded (FFPE) tissues. This antibody can be visualized using *ultra*View Universal DAB Detection Kit (Cat. No. 760-500 / 05269806001) and OptiView DAB IHC Detection Kit (Cat. No. 760-700 / 06396500001). Refer to the respective method sheet for further information.

MATERIAL PROVIDED

CONFIRM anti-PSA antibody contains sufficient reagent for staining 50 slides.

One 5 mL dispenser of CONFIRM anti-PSA antibody contains approximately 3.5 µg of a rabbit polyclonal antibody.

The antibody is diluted in Tris-HCl with a carrier protein, and 0.10% ProClin 300, a preservative.

Specific antibody concentration is approximately 0.7 µg/mL. There is no known non-specific antibody reactivity observed in this product.

There is a trace (~0.5%) of bovine serum albumin of U.S. origin from the stock solution.

Refer to the appropriate VENTANA detection kit method sheet for detailed descriptions of: Principle of the Procedure, Material and Methods, Specimen Collection and Preparation for Analysis, Quality Control Procedures, Troubleshooting, Interpretation of Results, and Limitations.

MATERIALS REQUIRED BUT NOT PROVIDED

Staining reagents, such as VENTANA detection kits and ancillary components, including negative and positive tissue control slides, are not provided.

Not all products listed in the method sheet may be available in all geographies. Consult your local support representative.

The following reagents and materials may be required for staining but are not provided:

1. Recommended control tissue
2. Microscope slides, positively charged
3. CONFIRM Negative Control Rabbit Ig (Cat. No. 760-1029 / 05266238001)
4. *ultra*View Universal DAB Detection Kit (Cat. No. 760-500 / 05269806001)
5. OptiView DAB IHC Detection Kit (Cat. No. 760-700 / 06396500001)
6. EZ Prep Concentrate (10X) (Cat. No. 950-102 / 05279771001)
7. Reaction Buffer Concentrate (10X) (Cat. No. 950-300 / 05353955001)
8. LCS (Predilute) (Cat. No. 650-010 / 05264839001)
9. ULTRA LCS (Predilute) (Cat. No. 650-210 / 05424534001)
10. Cell Conditioning Solution (CC1) (Cat. No. 950-124 / 05279801001)
11. ULTRA Cell Conditioning Solution (ULTRA CC1) (Cat. No. 950-224 / 05424569001)
12. Hematoxylin II (Cat. No. 790-2208 / 05277965001)
13. Bluing Reagent (Cat. No. 760-2037 / 05266769001)
14. Permanent mounting medium
15. Cover glass
16. Automated coverslipper
17. General purpose laboratory equipment
18. BenchMark IHC/ISH instrument

STORAGE AND STABILITY

Upon receipt and when not in use, store at 2-8°C. Do not freeze.

To ensure proper reagent delivery and the stability of the antibody, replace the dispenser cap after every use and immediately place the dispenser in the refrigerator in an upright position.

Every antibody dispenser is expiration dated. When properly stored, the reagent is stable to the date indicated on the label. Do not use reagent beyond the expiration date.

SPECIMEN PREPARATION

Routinely processed FFPE tissues are suitable for use with this primary antibody when used with VENTANA detection kits and BenchMark IHC/ISH instruments. The recommended tissue fixative is 10% neutral buffered formalin.[11] Sections should be cut at approximately 4 µm in thickness and mounted on positively charged slides. Slides should be stained immediately, as antigenicity of cut tissue sections may diminish over time.

Ventana recommends the use of positively charged microscope slides.

It is recommended that positive and negative controls be run simultaneously with unknown specimens.

WARNINGS AND PRECAUTIONS

1. For in vitro diagnostic (IVD) use.
2. For professional use only.
3. **CAUTION:** In the United States, Federal law restricts this device to sale by or on the order of a physician. (Rx Only)
4. Do not use beyond the specified number of tests.
5. ProClin 300 solution is used as a preservative in this reagent. It is classified as an irritant and may cause sensitization through skin contact. Take reasonable precautions when handling. Avoid contact of reagents with eyes, skin, and mucous membranes. Use protective clothing and gloves.

6. Positively charged slides may be susceptible to environmental stresses resulting in inappropriate staining. Ask your Roche representative for more information on how to use these types of slides.
7. This product contains 1% or less bovine serum albumin which is used in the manufacture of the antibody.
8. Materials of human or animal origin should be handled as biohazardous materials and disposed of with proper precautions. In the event of exposure, the health directives of the responsible authorities should be followed.[12,13]
9. Avoid contact of reagents with eyes and mucous membranes. If reagents come in contact with sensitive areas, wash with copious amounts of water.
10. Avoid microbial contamination of reagents as it may cause incorrect results.
11. For further information on the use of this device, refer to the BenchMark IHC/ISH instrument User Guide, and the instructions for use of all necessary components located at dialog.roche.com.
12. Consult local and/or state authorities with regard to recommended method of disposal.
13. Product safety labeling primarily follows EU GHS guidance. Safety data sheet available for professional user on request.
14. To report suspected serious incidents related to this device, contact the local Roche representative and the competent authority of the Member State or Country in which the user is established.

This product contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Table 1. Hazard information.

Hazard	Code	Statement
Warning 	H317	May cause an allergic skin reaction.
	H412	Harmful to aquatic life with long lasting effects.
	P261	Avoid breathing dust/ fume/ gas/ mist/ vapours/ spray.
	P273	Avoid release to the environment.
	P280	Wear protective gloves.
	P333 + P313	If skin irritation or rash occurs: Get medical advice/attention.
	P362 + P364	Take off contaminated clothing and wash it before reuse.
	P501	Dispose of contents/container to an approved waste disposal plant.

This product contains CAS # 55965-84-9, reaction mass of: 5-chloro-2-methyl-2H-isothiazol-3-one and 2-methyl-2H-isothiazol-3-one (3:1).

STAINING PROCEDURE

VENTANA primary antibodies have been developed for use on BenchMark IHC/ISH instruments in combination with VENTANA detection kits and accessories. Refer to Table 2 and Table 3 for recommended staining protocols.

This antibody has been optimized for specific incubation times but the user must validate results obtained with this reagent.

The parameters for the automated procedures can be displayed, printed, and edited according to the procedure in the instrument User Guide. Refer to the appropriate VENTANA detection kit method sheet for more details regarding immunohistochemistry staining procedures.

For more details on the proper use of this device, refer to the inline dispenser method sheet associated with P/N 760-2506.

Table 2. Recommended staining protocols for CONFIRM anti-PSA antibody with *ultra*View Universal DAB Detection Kit on BenchMark IHC/ISH instruments.

Procedure Type	Method		
	GX	XT	ULTRA or ULTRA PLUS [a]
Deparaffinization	Selected	Selected	Selected
Cell Conditioning (Antigen Unmasking)	CC1, mild	CC1, mild	ULTRA CC1, mild
Antibody (Primary)	8 minutes, 37°C	12 minutes, 37°C	16 minutes, 36°C
Counterstain	Hematoxylin II, 4 minutes		
Post Counterstain	Bluing, 4 minutes		

[a] Concordance was demonstrated between BenchMark ULTRA and BenchMark ULTRA PLUS instruments using representative assays.

Table 3. Recommended staining protocols for CONFIRM anti-PSA antibody with OptiView DAB IHC Detection Kit on BenchMark IHC/ISH instruments.

Procedure Type	Method		
	GX	XT	ULTRA or ULTRA PLUS [a]
Deparaffinization	Selected	Selected	Selected
Cell Conditioning (Antigen Unmasking)	CC1, 16 minutes	CC1, 16 minutes	ULTRA CC1, 16 minutes, 100°C
Pre Primary Peroxidase Inhibitor	Selected	Selected	Selected
Antibody (Primary)	8 minutes, 37°C	8 minutes, 37°C	8 minutes, 36°C
OptiView HQ Linker	8 minutes (default)		
OptiView HRP Multimer	8 minutes (default)		
Counterstain	Hematoxylin II, 4 minutes		
Post Counterstain	Bluing, 4 minutes		

[a] Concordance was demonstrated between BenchMark ULTRA and BenchMark ULTRA PLUS instruments using representative assays.

Due to variation in tissue fixation and processing, as well as general lab instrument and environmental conditions, it may be necessary to increase or decrease the primary antibody incubation, cell conditioning or protease pretreatment based on individual specimens, detection used, and reader preference. For further information on fixation variables, refer to "Immunohistochemistry Principles and Advances."[14]

NEGATIVE REAGENT CONTROL

In addition to staining with CONFIRM anti-PSA antibody, a second slide should be stained with the appropriate negative control reagent.

POSITIVE TISSUE CONTROL

Optimal laboratory practice is to include a positive control section on the same slide as the patient tissue. This helps identify failures applying reagents to the slide. Tissue with weak positive staining is best suited for quality control. Control tissue may contain both positive and negative staining elements and serve as both the positive and negative control tissue. Control tissue should be fresh autopsy, biopsy, or surgical specimen, prepared or fixed as soon as possible in a manner identical to the test sections.

Known positive tissue controls should be utilized only for monitoring performance of reagents and instruments, not as an aid in determining a specific diagnosis of test samples. If the positive tissue controls fail to demonstrate positive staining, results of the test specimen should be considered invalid.

An example of positive control tissue for CONFIRM anti-PSA antibody is normal prostate. Positive cytoplasmic staining in the secretory epithelial cells of the prostatic acini should be observed in normal prostate.

STAINING INTERPRETATION / EXPECTED RESULTS

The cellular staining pattern for CONFIRM anti-PSA antibody is cytoplasmic. See Figure 1 for an example of cytoplasmic staining in prostate carcinoma.

SPECIFIC LIMITATIONS

OptiView detection system is generally more sensitive than *ultra*View Universal DAB Detection Kit. The user must validate the results obtained with this reagent and detection systems.

All assays might not be registered on every instrument. Please contact your local Roche representative for more information.

PERFORMANCE CHARACTERISTICS

ANALYTICAL PERFORMANCE

Staining tests for sensitivity, specificity, precision, and method comparison were conducted and the results are listed below.

Sensitivity and Specificity

Table 4. Sensitivity/Specificity of CONFIRM anti-PSA antibody was determined by testing FFPE normal tissues.

Tissue	# positive / total cases	Tissue	# positive / total cases
Cerebrum	0/3	Bone marrow	0/3
Cerebellum	0/3	Lung	0/3
Adrenal gland	0/3	Heart	0/3
Ovary	0/3	Esophagus	0/3
Pancreas	0/3	Stomach	0/3
Parathyroid gland	0/3	Small intestine	0/3
Pituitary gland	0/3	Colon	0/3
Testis	0/3	Liver	0/3
Thyroid	0/3	Salivary gland [a]	3/3
Breast	0/3	Kidney	0/3
Spleen	0/3	Prostate [b]	10/10
Tonsil	0/3	Prostate hyperplasia	77/77
Endometrium	0/3	Cervix	0/3
Skeletal muscle	0/3	Skin	0/3
Nerve	0/3	Mesothelium	0/4
Lymph node	0/3	Bladder [c]	1/11
Thymus	0/3		

[a] Striated duct epithelial cells staining (luminal staining);
[b] Glandular epithelial cells staining;
[c] Umbrella cells staining

Table 5. Sensitivity/Specificity of CONFIRM anti-PSA antibody was determined by testing a variety of FFPE neoplastic tissues.

Pathology	# positive / total cases
Glioblastoma (Cerebrum)	0/1
Meningioma (Cerebrum)	0/1
Ependymoma (Cerebrum)	0/1
Oligodendroglioma (Cerebrum)	0/1
Serous carcinoma (Ovary)	0/2
Neuroendocrine neoplasm (Pancreas)	0/1
Adenocarcinoma (Pancreas)	0/1
Seminoma (Testis)	0/1
Embryonal carcinoma (Testis)	0/1
Medullary carcinoma (Thyroid)	0/1
Papillary carcinoma (Thyroid)	0/1
Invasive ductal carcinoma (Breast)	0/3
Small cell carcinoma (Lung)	0/1
Squamous cell carcinoma (Lung)	0/1
Adenocarcinoma (Lung)	0/1
Squamous cell carcinoma (Esophagus)	0/1
Adenocarcinoma (Esophagus)	0/1
Mucinous adenocarcinoma (Stomach)	0/1
Gastrointestinal stromal tumor (GIST) (Small Intestine)	0/1
Gastrointestinal stromal tumor (GIST) (Colon)	0/1
Gastrointestinal stromal tumor (GIST) (Rectum)	0/1
Adenocarcinoma (Gastrointestinal)	0/3
Hepatocellular carcinoma (Liver)	0/1
Hepatoblastoma (Liver)	0/1
Clear cell carcinoma (Kidney)	0/1
Adenocarcinoma (Prostate)	72/72
Prostatic adenocarcinoma (Metastatic)	10/10
Leiomyoma (Uterus)	0/1
Adenocarcinoma (Uterus)	0/1
Clear cell carcinoma (Uterus)	0/1
Squamous cell carcinoma (Cervix)	0/2
Embryonal rhabdomyosarcoma (Striated muscle)	0/1
Melanoma (Rectum)	0/1
Basal cell carcinoma (Skin)	0/1
Squamous cell carcinoma (Skin)	0/1
Neurofibroma (Lumbar)	0/1

Pathology	# positive / total cases
Neuroblastoma (Retroperitoneum)	0/1
Mesothelioma (Peritoneum)	0/1
B-Cell Lymphoma; NOS (Lymph node)	0/3
Hodgkin lymphoma (Lymph node)	0/1
Urothelial carcinoma (Bladder) [a]	1/39
Squamous cell carcinoma (Bladder)	0/1
Adenocarcinoma (Bladder)	0/1
Leiomyosarcoma (Bladder)	0/1
Leiomyosarcoma (Prostate)	0/4
Leiomyosarcoma (Smooth muscle)	0/1
Spindle cell rhabdomyosarcoma (Peritoneum)	0/1

[a] Focal staining

Precision

Precision studies for CONFIRM anti-PSA antibody were completed to demonstrate:

- Between lot precision of the antibody.
- Within run and between day precision on a BenchMark ULTRA instrument.
- Between instrument precision on the BenchMark GX, BenchMark XT, and BenchMark ULTRA instrument.
- Between platform precision between the BenchMark GX, BenchMark XT, and BenchMark ULTRA instrument.

All studies met their acceptance criteria.

Precision on the BenchMark ULTRA PLUS instrument was demonstrated using representative assays. Studies included Within-run Repeatability, Between-day and Between-run Intermediate Precision. All studies met their acceptance criteria.

CLINICAL PERFORMANCE

Clinical performance data relevant to the intended purpose of CONFIRM anti-PSA antibody were assessed by systematic review of the literature. The data gathered support the use of the device in accordance with its intended purpose.

REFERENCES

1. Dabbs DJ. Diagnostic Immunohistochemistry: Theranostic and Genomic Applications. Elsevier; 2018.
2. Krishna M. Diagnosis of Metastatic Neoplasms: An Immunohistochemical Approach. Arch Pathol Lab Med. 2010;134(2):207-215.
3. Chuang AY, DeMarzo AM, Veltri RW, et al. Immunohistochemical Differentiation of High-Grade Prostate Carcinoma from Urothelial Carcinoma. Am J Surg Pathol. 2007;31(8):1246-1255.
4. Queisser A, Hagedorn SA, Braun M, et al. Comparison of Different Prostatic Markers in Lymph Node and Distant Metastases of Prostate Cancer. Modern Pathology. 2014;28(1):138-145.
5. Sheridan T, Herawi M, Epstein JI, et al. The Role of P501s and Psa in the Diagnosis of Metastatic Adenocarcinoma of the Prostate. Am J Surg Pathol. 2007;31(9):1351-1355.
6. Fizazi K, Greco FA, Pavlidis N, et al. Cancers of Unknown Primary Site: Esmo Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up. Annals of Oncology. 2015;26(suppl 5):v133-v138.
7. Genega EM, Hutchinson B, Reuter VE, et al. Immunophenotype of High-Grade Prostatic Adenocarcinoma and Urothelial Carcinoma. Modern Pathology. 2000;13(11):1186-1191.
8. Kunju LP, Mehra R, Snyder M, et al. Prostate-Specific Antigen, High-Molecular-Weight Cytokeratin (Clone 34βe12), and/or P63. Am J Clin Pathol. 2006;125(5):675-681.
9. Mhawech P, Uchida T, Pelte M-F. Immunohistochemical Profile of High-Grade Urothelial Bladder Carcinoma and Prostate Adenocarcinoma. Hum Pathol. 2002;33(11):1136-1140.
10. Oh WJ, Chung AM, Kim JS, et al. Differential Immunohistochemical Profiles for Distinguishing Prostate Carcinoma and Urothelial Carcinoma. J Pathol Transl Med. 2016;50(5):345-354.
11. Sheehan DC, Hrapchak BB. Theory and Practice of Histotechnology, 2nd Edition. The C.V. Mosby Company, St. Louis, 1980.
12. Occupational Safety and Health Standards: Occupational exposure to hazardous chemicals in laboratories. (29 CFR Part 1910.1450). Fed. Register.
13. Directive 2000/54/EC of the European Parliament and Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work.
14. Roche PC, Hsi ED. Immunohistochemistry-Principles and Advances. Manual of Clinical Laboratory Immunology, 6th edition. (NR Rose Ed.) ASM Press, 2002.

NOTE: A point (period/stop) is always used in this document as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

The summary of safety and performance can be found here:

https://ec.europa.eu/tools/eudamed

Symbols

Ventana uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see dialog.roche.com for definition of symbols used):

GTIN	Global Trade Item Number
UDI	Unique Device Identification
	Indicates the entity importing the medical device into the European Union

REVISION HISTORY

Rev	Updates
H	Updates to Intended Use, Principle of the Procedure, Material Provided, Specimen Preparation, Warnings and Precautions, Staining Procedure, Negative Reagent Control and Analytical Performance sections. Added BenchMark ULTRA PLUS instrument.

INTELLECTUAL PROPERTY

CONTACT INFORMATION

Ventana Medical Systems, Inc.
1910 E. Innovation Park Drive
Tucson, Arizona 85755
USA
+1 520 887 2155
+1 800 227 2155 (USA)

www.roche.com

EC REP

Roche Diagnostics GmbH
Sandhofer Strasse 116
D-68305 Mannheim
Germany
+800 5505 6606

CE 0123