Negative Control (Monoclonal)

REF 760-2014

05266670001

IVD Σ 250

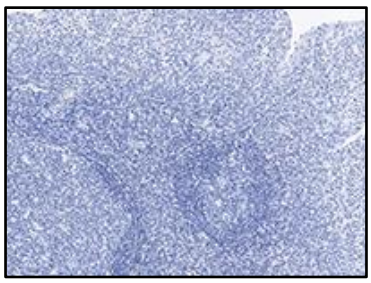

Figure 1. Negative Control (Monoclonal) antibody on tonsil.

INTENDED USE

Negative Control (Monoclonal) is intended for laboratory use as a control for the non-specific binding of mouse immunoglobulin 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

Negative Control (Monoclonal) antibody produced from clone MOPC21 is directed against an epitope not known to be present in human tissues.[1]

Negative Control (Monoclonal) antibody may be used to aid in the identification of cells or tissue components that bind to antibodies in an antigen independent manner. Negative Control (Monoclonal) antibody may demonstrate non-specific binding to constituents located in the cell membrane, cytoplasm, nucleus, or extracellular regions of normal and abnormal tissues. Non-specific antibody binding or interaction may occur, especially in neoplasms and necrotic tissue.

PRINCIPLE OF THE PROCEDURE

Negative Control (Monoclonal) antibody may be used in place of the primary antibody as a negative control for immunohistochemical staining of formalin-fixed, paraffin-embedded (FFPE) tissue sections. In general, immunohistochemical staining allows the visualization of antigens via the sequential application of a specific antibody (primary antibody) to the antigen, a secondary antibody (link antibody) to the primary antibody, an enzyme complex and a chromogenic substrate with interposed washing steps. The enzymatic activation of the chromogen results in a visible reaction product at the antigen site. The specimen may then be counterstained and cover slipped. Results are interpreted using light microscopy.

Negative Control (Monoclonal) antibody is optimally diluted for use with VENTANA detection kits and BenchMark IHC/ISH instruments. Each step in the staining protocol includes incubation for a precise time at a specific temperature. At the end of each incubation step, the sections are rinsed by the BenchMark IHC/ISH instrument to stop the reaction and remove unbound material that would hinder the desired reaction in subsequent steps. To minimize evaporation of the aqueous reagents from the specimen containing slide, liquid coverslip is applied in the instrument. Staining is completed after incubation with a substrate chromogen and optional counterstaining. For more detailed information on instrument operation, refer to the appropriate BenchMark IHC/ISH instrument User Guide.

MATERIAL PROVIDED

Negative Control (Monoclonal) antibody contains sufficient reagent for 250 tests.

One 25 mL dispenser of Negative Control (Monoclonal) antibody contains approximately 25 µg of a mouse monoclonal antibody.

The antibody is diluted in phosphate buffered saline containing carrier protein, and 0.05% ProClin 300, a preservative.

Specific antibody concentration is approximately 1 µg/mL.

Negative Control (Monoclonal) antibody is a mouse monoclonal antibody produced as ascites material.

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. Primary antibody
2. Recommended control tissue
3. Microscope slides, positively charged
4. OptiView DAB IHC Detection Kit (Cat. No. 760-700 / 06396500001)
5. OptiView Amplification Kit (Cat. No. 760-099 / 06396518001)
6. *ultra*View Universal DAB Detection Kit (Cat. No. 760-500 / 05269806001)
7. *ultra*View Universal Alkaline Phosphatase Red Detection Kit (Cat. No. 760-501 / 05269814001)
8. Amplification Kit (Cat. No. 760-080 / 05266114001)
9. Protease 1 (Cat. No. 760-2018 / 0566688001)
10. Protease 2 (Cat No. 760-2019 / 05266696001)
11. Protease 3 (Cat No. 760-2020 / 05266718001)
12. EZ Prep Concentrate (10X) (Cat. No. 950-102 / 05279771001)
13. Reaction Buffer Concentrate (10X) (Cat. No. 950-300 / 05353955001)
14. Antibody Diluent (Cat. No. 251-018 / 05261899001)
15. LCS (Predilute) (Cat. No. 650-010 / 05264839001)
16. ULTRA LCS (Predilute) (Cat. No. 650-210 / 05424534001)
17. Cell Conditioning Solution (CC1) (Cat. No. 950-124 / 05279801001)
18. Cell Conditioning Solution (CC2) (Cat. No. 950-123 / 05279798001)
19. ULTRA Cell Conditioning Solution (ULTRA CC1) (Cat. No. 950-224 / 05424569001)
20. ULTRA Cell Conditioning Solution (ULTRA CC2) (Cat. No. 950-223 / 05424542001)
21. Hematoxylin II (Cat. No. 790-2208 / 05277965001)
22. Bluing Reagent (Cat. No. 760-2037 / 05266769001)
23. General purpose laboratory equipment
24. 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 Negative Control (Monoclonal) antibody when used with VENTANA detection kits and BenchMark IHC/ISH instruments.

The recommended tissue fixative is 10% neutral buffered formalin.[2] 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. Ask your Roche representative for a copy of “Recommended Slide Storage and Handling” for more information.

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. 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.[3,4]
8. Avoid contact of reagents with eyes and mucous membranes. If reagents come in contact with sensitive areas, wash with copious amounts of water.
9. Avoid microbial contamination of reagents as it may cause incorrect results.
10. For further information on the use of this device, refer to the BenchMark IHC/ISH instrument User Guide, and instructions for use of all necessary components located at dialog.roche.com.
11. Consult local and/or state authorities with regard to recommended method of disposal.
12. Product safety labeling primarily follows EU GHS guidance. Safety data sheet available for professional user on request.
13. 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.
	P261	Avoid breathing mist or vapours.
	P272	Contaminated work clothing should not be allowed out of the workplace.
	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

Negative Control (Monoclonal) has been developed for use on BenchMark IHC/ISH instruments in combination with VENTANA detection kits and accessories. Refer to the appropriate primary antibody method sheet for the staining protocol. Negative Control (Monoclonal) antibody should be used in place of the primary antibody in the staining protocol to allow assessment of background staining within the tissue.

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 760-2014.

SPECIFIC LIMITATIONS

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

Under harsh antigen retrieval conditions (e.g., Protease 1 digestion), and longer antibody incubation times using the OptiView DAB IHC Detection Kit and OptiView Amplification Kit, this product may exhibit specific off target staining. Under these extreme conditions, epitopes may be unmasked which are partially recognized by Negative Control (Monoclonal) antibody. Weak interactions may be amplified by the use of the OptiView Amplification Kit.

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, and precision were conducted and the results are listed below.

Sensitivity and Specificity

Negative Control (Monoclonal) antibody is used as a negative control reagent for primary antibody assays on BenchMark IHC/ISH instruments. The sensitivity and specificity of Negative Control (Monoclonal) antibody was assessed in combination with a variety of mouse monoclonal primary antibodies using various staining protocols. The following performance characteristics were demonstrated:

1. Sensitivity and specificity of Negative control (Monoclonal) across a range of normal and neoplastic tissue types, and assay specific target tissues. Appropriate negative staining and acceptable background staining was observed.
2. Appropriate negative staining results and acceptable background were observed when the antibody was tested using several cell conditioning protocols such as CC1 cell conditioning selected from 8 to 92 minutes, or CC1 cell conditioning selected for 36 minutes in combination with Protease 3 digestion for 4 minutes and when an antibody incubation time from 8 to 32 minutes was selected.
3. Appropriate staining results were obtained with the OptiView DAB IHC Detection Kit, *ultra*View Universal DAB Detection Kit, and *ultra*View Universal Alkaline Phosphatase Red Detection Kit. However, excessive protease pretreatment (Protease 1 for 8 minutes), with longer antibody incubation times (32 minutes) in combination with OptiView DAB IHC Detection Kit and OptiView Amplification Kit lead to Negative Control (Monoclonal) antibody exhibiting off target staining in a variety of tissue types.

Precision

Precision studies for the Negative Control (Monoclonal) 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, BenchMark ULTRA instrument.
- Between platform precision between the BenchMark GX, BenchMark XT, BenchMark ULTRA instrument.

All studies were performed with the OptiView DAB IHC Detection Kit, *ultra*View Universal DAB Detection Kit, and *ultra*View Universal Alkaline Phosphatase Red Detection Kit using 64 minutes (or Standard) Cell Conditioning 1, and 16 minutes of antibody incubation.

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.

REFERENCES

1. Potter M. Immunoglobulin-Producing Tumors and Myeloma Proteins of Mice. Physiol Rev 52(3): 631-719, 1972.
2. Carson F, Hladik C. Histotechnology: A Self Instructional Text, 3rd edition. Hong Kong: American Society for Clinical Pathology Press; 2009.
3. Occupational Safety and Health Standards: Occupational exposure to hazardous chemicals in laboratories. (29 CFR Part 1910.1450). Fed. Register.
4. 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.

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.

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
C	Updates to Intended Use, Summary and Explanation, Principle of the Procedure, Material Provided, Materials Required But Not Provided, Storage and Stability, Specimen Preparation, Warnings and Precautions, Staining Procedure, Specific Limitations, Analytical Performance, Troubleshooting, References, Symbols, Intellectual Property, and Contact Information. 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