VENTANA ISH *i*VIEWBlue Detection Kit

REF 800-092

05278511001

IVD Σ 200

INTENDED USE

VENTANA ISH *i*VIEW Blue Detection Kit is an indirect biotin streptavidin system for the detection of fluorescein-labeled probes. The kit is intended to identify targets by in situ hybridization in sections of formalin-fixed, paraffin-embedded tissue that are 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 product is intended for in vitro diagnostic (IVD) use.

SUMMARY AND EXPLANATION

In general, in situ hybridization (ISH) uses labeled probes to detect specific DNA or RNA target sequences in fixed tissue specimens. Target sequences are exposed by heating the tissue and probe solution to denature nucleic acids. The reaction is then cooled allowing the labeled nucleic acid probe to hybridize to its complementary nucleic acid sequence in the tissue.

The hybridization of the probe to the nucleic acid sequence is visualized with an indirect detection method. A common indirect technique uses a biotinylated secondary antibody directed against the species of the primary anti-hapten antibody, and an enzyme linked with a corresponding substrate-chromogen system. This combination results in a colored precipitate at the site of specific antibody binding. The VENTANA ISH *i*VIEW Blue Detection Kit uses this indirect method to visualize complementary nucleic acid sequences by depositing a blue colored precipitate.

PRINCIPLE OF THE PROCEDURE

VENTANA ISH *i*VIEW Blue Detection Kit detects specific fluorescein-labeled probes bound to specific target sequences in formalin-fixed, paraffin-embedded (FFPE) tissue sections. VENTANA ISH *i*VIEW Blue Detection Kit contains mouse anti-fluorescein primary antibody that detects the fluorescein-labeled probes bound to the target sequence. The anti-fluorescein antibody is followed by the binding of a biotinylated secondary antibody consisting of goat anti mouse IgG. This step is followed by the addition of a Streptavidin-AP (alkaline phosphatase) enzyme conjugate which binds to the biotin present on the secondary antibody. The complex is then visualized with 5-Bromo-4-chloro-3-indolyl phosphate (BCIP) and nitro blue tetrazolium (NBT) chromogen, which produces a blue precipitate that is readily detected by light microscopy.

Unlike horseradish peroxidase, alkaline phosphatase is unaffected by endogenous peroxidase activity and is therefore more effective for labeling specimens heavily infiltrated with neutrophils or eosinophils. Nitro blue tetrazolium stains the tissue blue and has the advantages of a higher extinction coefficient, yielding a more intense color reaction at the site of probe target interaction.

The staining protocol consists of numerous steps in which reagents are incubated for pre-determined times at specific temperatures. At the end of each incubation step, the BenchMark IHC/ISH instrument washes the sections to remove unbound material and applies a liquid coverslip which minimizes the evaporation of the aqueous reagents from the slide. Results are interpreted using a light microscope and aid in the differential diagnosis of pathophysiological processes, which may or may not be associated with positive staining for the probe.

For more detailed information on instrument operation, refer to the appropriate User Guide. Figure 1 illustrates the indirect detection method.

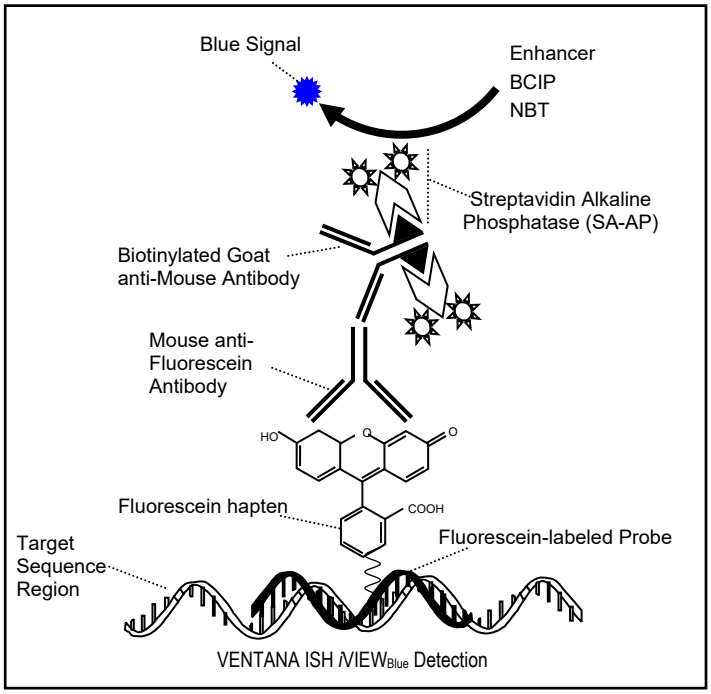

Figure 1. VENTANA ISH *i*VIEW *Blue* Detection Reaction

MATERIAL AND METHODS

Material Provided

VENTANA ISH *i*VIEW Blue Detection Kit contains sufficient reagent for 200 tests.

One 20 mL dispenser	VENTANA ISH *i*VIEW Blue Detection Kit contains approximately 0.5 µg/mL Anti-Fluorescein mouse monoclonal antibody in phosphate buffered saline with protein stabilizer and 0.10% ProClin 300, a preservative.
One 20 mL dispenser	VENTANA ISH *i*VIEW *Blue* Detection Kit Biotinylated Ig contains approximately 10 µg/mL affinity-purified goat anti mouse IgG in phosphate buffered saline with protein stabilizer and 0.10% ProClin 300, a preservative.
One 20 mL dispenser	VENTANA ISH *i*VIEW Blue Detection Kit Streptavidin Alkaline Phosphatase, approximately 1%, in Tris buffer with MgCl2 and ZnCl2 and 0.10% ProClin 300, a preservative.
One 20 mL dispenser	VENTANA ISH *i*VIEW Blue Detection Kit Enhancer contains approximately 11% v/v MgCl2 solution with 0.10% ProClin 300, a preservative.
One 20 mL dispenser	VENTANA ISH *i*VIEW Blue Detection Kit NBT contains nitro blue tetrazolium (0.5 g/L) in approximately 1% v/v dimethylformamide.
One 20 mL dispenser	VENTANA ISH *i*VIEW Blue Detection Kit BCIP contains 5-bromo-4-chloro-3-indolyl phosphate (0.5 g/L) in a Tris buffer.

Reconstitution, Mixing, Dilution, Titration

The detection kit is optimized for use on a BenchMark IHC/ISH instrument. No reconstitution, mixing, dilution, or titration of kit reagents is required. Further dilution may result in loss of staining.

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 with the detection kit:

1. ISH probe
2. Positive and negative tissue controls (consult probe method sheets for recommended types)
3. ISH Protease 1 (Cat. No. 780-4147 / 05273315001)
4. ISH Protease 2 (Cat. No. 780-4148 / 05273323001)
5. ISH Protease 3 (Cat. No. 780-4149 / 05273331001)
6. Red Counterstain II (Cat. No. 780-2218 / 05272017001)
7. Reaction Buffer Concentrate (10X) (Cat. No. 950-300 / 05353955001)
8. Negative Control Probe (Cat. No. 800-2847 / 05278716001)
9. SSC (10X) (Cat. No. 950-110 / 05353947001)
10. EZ Prep Concentrate (10X) (Cat. No. 950-102 / 05279771001)
11. Cell Conditioning Solution (CC1) (Cat. No. 950-124 / 05279801001)
12. Cell Conditioning Solution (CC2) (Cat. No. 950-123 / 05279798001)
13. ULTRA Cell Conditioning Solution (ULTRA CC1) (Cat. No. 950-224 / 05424569001)
14. ULTRA Cell Conditioning Solution (ULTRA CC2) (Cat. No. 950-223 / 05424542001)
15. LCS (Predilute) (Cat. No. 650-010 / 05264839001)
16. ULTRA LCS (Predilute) (Cat. No. 650-210 / 05424534001)
17. BenchMark IHC/ISH instrument
18. Permanent mounting medium
19. Coverslip sufficient to cover tissue
20. Automated coverslipper
21. Microscope slides, positively charged
22. General purpose laboratory equipment.

Storage and Stability

Upon receipt and when not in use, store at 2-8°C. Do not freeze. This detection kit can be used immediately after removal from the refrigerator.

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

Every detection kit is expiration dated. When properly stored, the reagents are stable to the date indicated on the label. Do not use product beyond the expiration date. There are no definitive signs to indicate instability of this product; therefore, positive and negative controls should be run simultaneously with unknown specimens. Your local support representative should be contacted immediately if unexpected results are observed.

Specimen Collection and Preparation for Analysis

Routinely processed FFPE tissues are suitable for the VENTANA ISH iVIEW Blue Detection Kit and BenchMark IHC/ISH instruments (see Materials Required but Not Provided section). The recommended tissue fixative is 10% neutral buffered formalin (NBF).[1] Variable results may occur as a result of tissue section thickness, fixation type, incomplete or prolonged fixation or special processes such as decalcification of bone marrow preparations.

Each section should be cut to the appropriate thickness (2-5 µm) for the probe being used and placed on a positively charged glass microscope slide. Slides should be drained or dried to remove excess water between slide and tissue. Slide heating may be used to further enhance tissue adhesion to the glass. Consult the probe method sheet to identify heating limitations.

Sections thicker than 4 µm may require stronger protease treatment than the recommended condition and may exhibit more nuclear bubbling than thinner sections due to excess paraffin in the tissue. Nuclear bubbling appears as large or small bubbles or vacuoles in the nuclei. Usually this artifact does not push the Blue ISH signals to the periphery of the nuclei or otherwise distort them, and therefore it does not interfere with signal enumeration. However, severe cases of nuclear bubbling may distort the nuclei or Blue ISH signals such that enumeration is not possible. These specimens may need to be deparaffinized in xylene and alcohol baths prior to repeat staining on the instrument, or the user may select the extended deparaffinization option in the staining procedure (see Troubleshooting). Nuclear bubbling also may occur in the context of underfixation (1-3 hours with formalin) which is typically a less discrete nuclear bubbling. This may be remedied for tissues fixed three hours with changed cell conditioning/protease treatment, but for those tissues fixed one hour are probably beyond remedy.

Properly fixed and embedded tissues expressing the RNA and DNA will remain stable if stored in a cool location (15-25°C). The Clinical Laboratory Improvement Act (CLIA) of 1988, 42CFR493.1259 (b) requires that "The laboratory must retain slides at least ten years from the date of examination and retain specimen blocks at least two years from date of examination." Each laboratory should validate the cut slide stability for their own procedures and environmental storage conditions.

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. **Warning, Product Contains Formamide**. Formamide is toxic by inhalation and moderately toxic by ingestion. It is an irritant to skin, eyes, and mucous membranes and is absorbed through the skin. It may cause harm to the unborn child. Take precautions when handling reagents. Use disposable gloves and wear suitable protective clothing when handling suspected carcinogens or toxic materials. Do not use beyond the specified number of tests.
5. Do not use beyond the specified number of tests.
6. ProClin 300 is used as a preservative in this solution. 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.
7. Materials of human or animal origin should be handled as potentially biohazardous and disposed of with proper precautions. In the event of exposure, the health directives of the responsible authorities should be followed.[2,3]
8. Take reasonable precautions when handling reagents. Avoid contact of reagents with eyes, skin, and mucous membranes. Use disposable gloves and wear suitable protective clothing when handling suspected carcinogens or toxic materials.
9. If reagents come in contact with sensitive areas, wash with copious amounts of water. Avoid inhalation of reagents.
10. Ensure that the waste container is empty prior to starting a run on the instrument. If this precaution is not taken, the waste container may overflow and the user risks a slip and fall.
11. Avoid microbial contamination of reagents as this may produce incorrect results.
12. For further information on the use of this device, refer to the BenchMark IHC/ISH instrument User Guide, and method sheets of all necessary components located at navifyportal.roche.com.
13. Consult local and/or state authorities to determine the recommended method of disposal.
14. Product safety labeling primarily follows EU GHS guidance. Safety data sheet available for professional user on request.
15. 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.

Table 1. Hazard information.

Hazard	Code	Statement
Danger 	H317	May cause an allergic skin reaction.
	H360D	May damage the unborn child
	H412	Harmful to aquatic life with long lasting effects.
	P201	Obtain special instructions before use
	P261	Avoid breathing mist or vapours.
	P273	Avoid release to the environment.
	P280	Wear protective gloves/ protective clothing/ eye protection/ face protection/ hearing protection.
	P308 + P313	IF exposed or concerned: Get medical advice/ attention.
	P333 + P313	If skin irritation or rash occurs: Get medical advice/ attention.

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).

PROCEDURE

The VENTANA ISH *i*VIEW Blue Detection Kit has been developed for use on BenchMark IHC/ISH instruments in combination with VENTANA ancillary reagents. The staining protocols can be displayed, printed and edited according to the procedure in the instrument User Guide. Other operating parameters for the instrument have been preset at the factory.

The procedures for staining on BenchMark IHC/ISH instruments are as follows. For more detailed instructions and additional protocol options refer to the appropriate probe method sheet or your User Guide.

BenchMark IHC/ISH Instruments

1. Apply slide bar code label which corresponds to the protocol to be performed.
2. Load the probe dispenser, appropriate detection kit dispensers, and required accessory reagent dispensers onto the reagent tray and place them on the instrument.
3. Check bulk fluids and empty waste.
4. Load the slides onto the instrument.
5. Start the staining run.
6. At the completion of the run, remove the slides from the instrument.
7. Proceed to Recommended Post-Instrument Processing Procedure.

Recommended Post-Instrument Processing Procedures

NOTE: To ensure complete dehydration, ethanol baths need to be changed frequently and a third 100% ethanol bath may be added.

1. To remove Liquid Coverslip solution, wash the slides in 2 sequential solutions of a mild dishwashing detergent (do not use detergent designed for automatic dishwashers).
2. Rinse slides well with distilled water, about 1 minute. Shake off excess water.
3. Transfer the slides to an 80 % ethanol bath for approximately 1 minute.
4. Transfer the slides to a 90 % ethanol bath for approximately 1 minute.
5. Transfer the slides to a 100 % ethanol bath for approximately 1 minute.
6. Transfer the slides into a second bath of 100 % ethanol for approximately 1 minute.
7. Dip slides 10 times into 100 % acetone (one time use only, replace acetone after each staining run). Do not leave slides in acetone.
8. Transfer the slides into the first xylene bath for approximately 30 seconds.
9. Transfer the slides into a second xylene bath for approximately 30 seconds.
10. Place coverslip on slide.

QUALITY CONTROL PROCEDURE

Positive Tissue Control

A positive tissue control must be run with every staining procedure performed. Optimal laboratory practice is to include a positive control section on the same slide as the patient tissue. The positive staining tissue components are used to confirm that the reagents were applied and the instrument functioned properly. This tissue may contain both positive and negative staining cells or tissue components and serve as both the positive and negative control tissue. Internal tissue controls are used at the discretion of the principal investigator and the pathologist. Control tissues should be autopsy, biopsy, or surgical specimens prepared or fixed in a manner identical to the test sections. Tissue sections fixed or processed differently from the test specimen will provide comparative controls for all reagents and method steps affected by fixation and tissue processing.

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

See appropriate probe package insert for specific positive tissue control recommendations.

Negative Tissue Control

A negative specimen control must be run with every staining procedure performed. The purpose is to monitor unintended probe cross reactivity to cellular components. The same specimen used for the positive specimen control may also be used as the negative specimen control. The variety of different cell types present in most specimens offers internal negative control sites, but this should be verified by the user. The non-staining components should demonstrate absence of specific staining and provide an indication of background staining. If unacceptable staining occurs in the negative specimen control sites, result with the patient specimens should be considered invalid.

If applicable, see appropriate probe method sheet.

Positive Reagent Control

Positive reagent control should be run during assay verification and troubleshooting since DNA and RNA accessibility may vary depending on fixation method and pretreatment of the specimen.

If applicable, see appropriate probe method sheet.

Negative Reagent Control

Negative reagent control must be substituted for the ISH probe with every specimen stained to aid in interpretation of each patient result. This provides an indication of nonspecific background staining for each slide. In place of the ISH probe, stain the slide with Negative Control Probe. The incubation period for controls should correspond to that of the probe.

The negative control is especially important with the finding that the intestinal form of alkaline phosphatase may be found in cells other than the brush border of intestinal epithelial cells.[4] Additionally, enzymes capable of reducing nitro blue tetrazolium may be preserved during fixation.[5,6]

Unexplained Discrepancies

Unexplained discrepancies in controls should be referred to your local support representative immediately. If quality control results do not meet specifications, patient results are invalid. See the Troubleshooting. Identify and correct the problem, then repeat the patient samples.

Assay Verification

Prior to initial use of a probe or staining system in a diagnostic procedure, the specificity of the probe should be verified by testing it on a series of tissues with known ISH performance characteristics (refer to the probe method sheet) and to the Quality Control recommendations of the College of American Pathologists Laboratory Accreditation Program, Anatomic Pathology Checklist,[7] or the CLSI Approved Guideline [8] or both documents). These quality control procedures should be repeated for each new lot or reagent, or whenever there is a change in assay parameters, or whenever there is a change in assay parameters.

Interpretation of Results

The VENTANA ISH *i*VIEW Blue Detection Kit causes a blue-colored reaction product to precipitate at the nucleic acid sequence hybridized by the probe. A qualified pathologist who is experienced in ISH procedures must evaluate controls and qualify the stained product before interpreting results. Staining of negative controls must be noted first, and

these results compared to the stained material to verify that the signal generated is not the result of nonspecific interactions.

LIMITATIONS

General Limitations

1. ISH is a multiple step methodology that requires specialized training in the selection of the appropriate reagents, specimen preparation, processing, preparation of the slide, and interpretation of the results.
2. Tissue staining is dependent on the handling and processing of the tissue prior to staining. Improper fixation, freezing, thawing, washing, drying, heating, sectioning, or contamination with other tissues or fluids may produce artifacts, reagent trapping, or false negative or false positive results. Inconsistent results may be a consequence of variations in fixation and embedding methods, or inherent irregularities within the tissue.
3. Excessive or incomplete counterstaining may compromise proper interpretation of results.
4. The clinical interpretation of any positive staining, or its absence, must be evaluated within the context of clinical history, morphology and other histopathological criteria. It is the responsibility of a qualified pathologist to be familiar with the reagents and methods used to produce the stained preparation. Staining must be performed in a certified, licensed laboratory under the supervision of a pathologist who is responsible for the review of the stained slides and assuring the adequacy of controls.
5. VENTANA reagents are provided at optimal dilution for use when the provided instructions are followed. Further dilution may result in loss of appropriate staining. Any deviation from recommended test procedures may invalidate expected results. Appropriate controls must be employed and documented. Users who deviate from recommended test procedures must accept responsibility for interpretation of patient results.
6. Reagents may demonstrate unexpected reactions in previously untested tissues. The possibility of unexpected reactions even in tested tissue groups cannot be completely eliminated because of biological variability of tissues. Contact your local support representative with documented unexpected reactions.

Specific Limitations

1. Each step of the detection kit procedure has been optimized on BenchMark IHC/ISH instruments and is preset. Because of variation in tissue fixation and processing, it may be necessary to increase or decrease the hybridization time on individual specimens. For further information on fixation variables, refer to "Immunohistochemistry Principles and Advances"[6] or "Immunomicroscopy: A Diagnostic Tool for the Surgical Pathologist."[9]
2. The detection kit, in combination with VENTANA probes and accessories, detects nucleic acid sequence that survives routine formalin fixation, tissue processing, and sectioning.
3. As with any test, a negative result means that the specific nucleic acid sequence was not detected, not that the specific nucleic acid sequence was absent in the cells or tissue assayed.
4. This detection kit has been optimized for use with Reaction Buffer wash solution, probes, accessories, and BenchMark ICH/ISH instruments. The use of Reaction Buffer wash solution is important to the proper function of the detection kit. Users who deviate from recommended test procedures are responsible for interpretation of patient results under these circumstances.
5. This detection kit has been optimized for use with LCS (Predilute) or ULTRA LCS (Predilute). LCS is a prediluted coverslip solution used both as a barrier between aqueous reagents and the air as well as a reagent to remove paraffin from tissue samples during the deparaffinization process. The LCS barrier reduces evaporation and provides a stable aqueous environment for the ISH reactions carried out on BenchMark IHC/ISH instruments.
6. When using fluorescein-labeled probes and the VENTANA ISH *i*VIEW Blue Detection Kit, cytoplasmic and/or nuclear staining in epithelial cells of gastrointestinal tissue may be observed. Use of the Negative Control Probe is required to detect this staining.
7. All detection kits might not be registered on every instrument. Please contact your local Roche representative for more information.

PERFORMANCE CHARACTERISTICS

The performance of the VENTANA ISH *i*VIEW Blue Detection Kit was evaluated through reproducibility and other relevant studies.

Multiple VENTANA probes have been developed with the VENTANA ISH *i*VIEW Blue Detection Kit. As part of the testing for those assays, the following performance characteristics were demonstrated for VENTANA ISH *i*VIEW Blue Detection Kit;

1. Within-run, between-day, between-instrument, and between-platform precision on the BenchMark IHC/ISH instruments.
2. Sensitivity and specificity of staining across a range of normal and neoplastic tissue types and assay-specific target tissues.

All studies met their acceptance criteria.

TROUBLESHOOTING

1. Refer to the Troubleshooting section of the appropriate probe method sheet.
2. Incomplete paraffin removal could result in staining artifacts or no staining.
   - If all paraffin has not been removed from the slide, the staining run should be repeated using the extended deparaffinization option, if available.
   - Alternatively, a manual off-instrument deparaffinization can be performed. If the manual option is used, deselect online deparaffinization from the staining protocol prior to loading the slides on the instrument. Extra care should be taken to ensure slides do not dry out prior to the staining run.
3. If tissue sections wash off the slide, slides should be checked to ensure that they are positively charged. Refer to the Specimen Collection and Preparation for Analysis section.
4. If sections thicker than 4 µm exhibit nuclear bubbling due to excess paraffin, select the "extended deparaffinization" option in the staining procedure.
5. For corrective action, refer to the instrument User Guide, or contact your local support representative.
6. If a reagent dispenser does not dispense fluid, check the priming chamber or meniscus for foreign materials or particulates, such as fibers or precipitates. If the dispenser is blocked, do not use the dispenser and contact your local support representative. Otherwise, re-prime the dispenser by aiming the dispenser over a waste container, removing the nozzle cap, and pressing down on the top of the dispenser. Refer to the associated inline dispenser method sheet for information about proper use.

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.

REFERENCES

1. Carson FL, Cappellano C. HIstotechnology; A Self-Instructional Text, 5th edition. American Society for Clinical Pathology Press; 2020, 2022.
2. Occupational Safety and Health Standards: Occupational exposure to hazardous chemicals in laboratories. (29 CFR Part 1910.1450). Fed. Register.
3. Directive 2000/54/EC of the European Parliament and Council of 24 June 2020 on the protection of workers from risks related to exposure to biological agents at work.
4. Doria M, Lloyd D, Thistlethwaite JR, Franklin WA. Immunohistochemical detection of antibody in tissue sections of non-perfused and ex vivo-perfused organs using a tetrazolium alkaline phosphatase substrate. Histochemistry. 1988;89(5):443-446.
5. True LD. Atlas of Diagnostic Immunohistopathology. J.B. Lippincott Co., Philadelphia, PA, 1990.
6. Roche PC, Hsi ED. Immunohistochemistry-Principles and Advances. Manual of Clinical Laboratory Immunology, 6th edition. In: NR Rose, ed. ASM Press; 2002.
7. College of American Pathologists Laboratory Accreditation Program, Anatomic Pathology Checklist, 2001.
8. CLSI (formerly NCCLS). Quality Assurance for Immunocytochemistry: Approved Guideline. CLSI document MM4-A- (ISBN 1-56238-396-5). CLSI, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA, 1999.
9. Taylor C, Cote RJ. Immunomicroscopy: A Diagnostic Tool for the Surgical Pathologist. 2nd Edition. Philadelphia, PA. W.B. Saunders Company; 1986.

NOTE: A point (period/stop) is always used in this document as the decimal separator to mark the order 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 elabdoc.roche.com/symbols for more information).

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

REVISION HISTORY

Rev	Updates
G	Updates to Materials Required But Not Provided section.

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

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

CE