VENTANA HE 600 Hematoxylin

REF 07024282001

IVD

INTENDED USE

VENTANA HE 600 Hematoxylin is intended for use as a qualitative histologic stain to demonstrate nucleic acid staining by light microscopy in sections of formalin-fixed, paraffin-embedded (FFPE) tissue stained on the VENTANA HE 600 system. The product should be interpreted by a qualified pathologist in conjunction with relevant clinical information, and proper controls.

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

PRINCIPLE OF THE PROCEDURE

VENTANA HE 600 Hematoxylin reagent is a progressive stain used for nuclear staining. Progressive staining is used to obtain the desired intensity without over staining. Progressive hematoxylin staining solutions do not require de-colorization of the tissue sections to differentiate the nuclear chromatin from other tissue entities. VENTANA HE 600 Hematoxylin reagent is used in conjunction with VENTANA HE 600 Bluing reagent and when applied to tissue sections will change the hue of hematoxylin from purple to blue.

The VENTANA HE 600 system is an automated, high-volume, hematoxylin and eosin (H&E) stainer. VENTANA HE 600 products, including staining reagents, ancillary solutions, and glass coverslips, are optimized for use on the VENTANA HE 600 system. VENTANA HE 600 products include all necessary reagents and ancillaries to achieve paraffin removal, staining, clearing, and coverslipping of FFPE tissue on glass microscope slides.

MATERIAL PROVIDED

One 2L bottle of VENTANA HE 600 Hematoxylin contains 6 g/L hematoxylin dye, 27 g/L aluminum sulfate, 9 g/L hydroquinone, 0.7 g/L sodium iodate, and beta-cyclodextrin hydrate in an aqueous ethylene glycol stabilizing solution.

Reconstitution, Mixing, Dilution, Titration

No reconstitution, mixing, dilution, or titration is required. Further dilution may result in loss of staining specificity.

MATERIALS REQUIRED BUT NOT PROVIDED

1. VENTANA HE 600 Eosin (REF 06544304001)
2. VENTANA HE 600 Differentiating Solution (REF 06544339001)
3. VENTANA HE 600 Bluing (REF 06544347001)
4. VENTANA HE 600 Organic Solution (REF 07095163001)
5. VENTANA HE 600 Transfer Fluid (REF 06544380001)
6. VENTANA HE 600 Wash (REF 06544312001)
7. VENTANA HE 600 Cleaning Solution (REF 07257538001)
8. VENTANA HE 600 Coverslip Activator (REF 07534396001)
9. VENTANA HE 600 Glass Coverslips (REF 06711138001)
10. VENTANA HE 600 system
11. General purpose laboratory equipment

STORAGE AND STABILITY

Upon receipt and when not in use, store at 15-30ºC. Keep out of direct sunlight. Do not freeze.

This product is expiration dated. When properly stored, the product is stable to the date indicated on the label. Do not use product beyond the expiration date.

When in use, the product expires after 28 days or the date indicated on the label.

SPECIMEN PREPARATION

Routinely processed, FFPE tissues are suitable for use with the VENTANA HE 600 system. The recommended tissue fixative is 10% neutral buffered formalin.[1]

See Table 1 for other fixatives.

Table 1. Supported fixatives for use with the VENTANA HE 600 system.

Fixative	Manufacturer
Acid Zinc Formalin	Newcomer Supply
Bouin's Solution	Richard-Allan Scientific
Fix-All	Surgipath
Shandon Glyo-Fixx	Thermo Fisher Scientific
GTF	StatLab
IBF	Surgipath
O-Fix	Surgipath
Stat-Fix	Surgipath
Z-5 (Z-Fix)	Anatec
Zinc Formalin	Polysciences, Inc.

WARNINGS AND PRECAUTIONS

1. For in vitro diagnostic (IVD) use.
2. For professional use only.
3. Materials of human or animal origin should be handled as potentially bio hazardous and disposed of with proper precautions. In the event of exposure, the health directives of the responsible authorities should be followed.[2,3]
4. Avoid contact of reagents with eyes and mucous membranes. If reagents come in contact with sensitive areas, wash with copious amounts of water.
5. Avoid microbial contamination of product, as this may cause incorrect results.
6. For further information on the use of this product, refer to the VENTANA HE 600 system User Guide, and instructions for use of all necessary components located at dialog.roche.com.
7. Consult local and/or state authorities with regard to recommended method of disposal.
8. Product safety labeling primarily follows EU GHS guidance. Safety data sheet available for professional user on request.
9. 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 2. Hazard information.

Hazard	Code	Statement
Warning 	H302	Harmful if swallowed.
	H319	Causes serious eye irritation.
	P264	Wash skin thoroughly after handling.
	P270	Do not eat, drink or smoke when using this product.
	P280	Wear eye protection/ face protection.
	P301 + P312 + P330	IF SWALLOWED: Call a POISON CENTER/doctor if you feel unwell. Rinse mouth.
	P337 + P313	If eye irritation persists: Get medical advice/attention.
	P501	Dispose of contents/ container to an approved waste disposal plant.
	EUH208	Contains hydroquinone. May produce an allergic reaction.

This product contains CAS # 107-21-1 ethane-1,2-diol.

PROCEDURE

This product has been developed for use on a VENTANA HE 600 system in combination with VENTANA HE 600 solutions and accessories.

VENTANA HE 600 Hematoxylin is loaded in the specified position in the automated fluidics module on the VENTANA HE 600 system. VENTANA HE 600 Hematoxylin is applied automatically as required for the procedure being run.

The parameters for the automated procedures can be displayed, printed and edited according to the procedure in the User Guide. Refer to the instrument User Guide for detailed instructions and additional protocol options.

Refer to the table below for concordance of levels and incubation times for the Hematoxylin, Differentiating Solution, and Eosin protocols.

Table 3. Concordance of Levels and incubation times on the VENTANA HE 600 system.

Protocol	Method	
Drying (optional)	Select to enable baking	
Hematoxylin	Level 1: lighter hematoxylin staining Level 10: darker hematoxylin staining	
Differentiation	Level 0: no reagent applied Level 5: greater differentiation for lightest hematoxylin staining (Hematoxylin level 1) Level 3: greater differentiation of nuclear and mucin staining (Hematoxylin level 2-10)	
Eosin	Level 1: lighter eosin staining Level 10: darker eosin staining	
Modified Eosin	Option 1: Transfer Fluid dispensed after eosin staining Option 2: Differentiating Solution dispensed after eosin staining Note: A Modified Eosin Option may be selected to improve consistency and amplify staining of cytoplasmic features.	
Coverslip (optional)	Select to enable coverslipping	
Reagent Options		
Hematoxylin	**Differentiation**	**Eosin**
Level / Incubation time	**Level / Incubation time (Hematoxylin level)**	**Level / Incubation time**
1 / 1 min	0 / 0 min (1)	1 / 0.5 min
2 / 2 min *	1 / 0.5 min (1) *	2 / 0.75 min
3 / 3 min	2 / 1 min (1)	3 / 1 min
4 / 4 min	3 / 1.5 min (1)	4 / 1.5 min
5 / 5 min	4 / 2 min (1)	5 / 2 min *
6 / 6 min	5 / 3 min (1)	6 / 3 min
7 / 7 min	0 / 0 min (2-10)	7 / 4 min
8 / 8 min	1 / 0.5 min (2-10)	8 / 5 min
9 / 9 min	2 / 1 min (2-10)	9 / 6 min
10 / 10 min	3 / 1.5 min (2-10)	10 / 7 min

*Default level / incubation time

SPECIFIC LIMITATIONS

Inconsistent staining of peri-implant granulation tissue on breast samples stained with VENTANA HE 600 system H&E has been reported. Specifically, there are focal areas of the granulation tissue that do not stain with eosin and/or hematoxylin. Based on a review of affected slides, this staining artifact is easily detectable by an appropriately trained pathologist or histology technician. The clinical interpretation of the absence of staining will need to be evaluated within the context of clinical history, morphology and other histopathological criteria. The user should validate the staining result when using this type of tissue on the VENTANA HE 600 system.

PERFORMANCE CHARACTERISTICS

ANALYTICAL PERFORMANCE

VENTANA HE 600 Hematoxylin was tested on the VENTANA HE 600 system using over 75 types of tissues.

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

Sensitivity and Specificity

For a hematoxylin and eosin stain, analytical specificity is assessed by the ability of the product to appropriately stain various tissue structures. For hematoxylin, this includes appropriate staining of nuclear material. For eosin, this includes appropriate staining of eosinophilic structures. For both hematoxylin and eosin, non-specific staining must be minimized in order to maximize analytical specificity. The staining attributes that affect analytical specificity are: eosin intensity, eosin hue, eosin, differentiation, hematoxylin intensity, hematoxylin hue, and hematoxylin differentiation.

Analytical sensitivity can be assessed by the ability of the product to correctly stain (correct stain hue) elements in a particular tissue sample. The staining attributes that affect analytical sensitivity are: eosin intensity, eosin hue, hematoxylin intensity, and hematoxylin hue. The various staining attributes assessed are summarized in Table 4.

Table 4. Sensitivity/Specificity of the H&E slide staining on the VENTANA HE 600 system.

Parameters Tested	% Pass Rate (passed/stained)
Eosin intensity	100% (5266/5266)
Eosin hue	100% (5266/5266)
Eosin differentiation	100% (5266/5266)
Hematoxylin intensity	100% (5266/5266)
Hematoxylin hue	100% (5266/5266)
Hematoxylin differentiation	100% (5266/5266)

Precision

Acceptable reproducibility and repeatability of the staining was demonstrated for the VENTANA HE 600 system, and the results are listed in Table 5.

Table 5. Precision slide studies of the H&E staining on the VENTANA HE 600 system.

Parameters Tested	# of Conditions	% Pass Rate (passed/stained)
Study 1		
Run to Run	164 runs	99.7% (2663/2672)
Day to Day	11 days	99.7% (2663/2672)
Instrument to Instrument	4 instruments	100% (709/709); 99.6% (692/695); 100% (524/524); 99.4% (722/726)

Parameters Tested	# of Conditions	% Pass Rate (passed/stained)
Intra Run	164 runs	No runs with > 2 failures
Study 2		
Run to Run	161 runs	99.7% (2585/2594)
Day to Day	17 days	99.7% (2585/2594)
Instrument to Instrument	3 instruments	100% (767/767); 99.3% (862/868); 99.7% (956/959)
Intra Run	161 runs	No runs with > 2 failures

Lot-to-lot reproducibility: 5 lots of VENTANA HE 600 Hematoxylin were tested across 6 VENTANA HE 600 systems using a total of 5266 slides. The H&E slides were evaluated for staining with a 99.7% pass rate.

The results demonstrated no significant difference in staining intensity among the slides.

TROUBLESHOOTING

For corrective action, refer to the VENTANA HE 600 system User Guide or contact your local support representative.

REFERENCES

1. Carson F, Hladik C. Histotechnology: A Self Instructional Text, 3rd edition. Hong Kong: American Society for Clinical Pathology Press; 2009.
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 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

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