VENTANA anti-Helicobacter pylori (SP48) Rabbit Monoclonal Primary Antibody

REF 790-1014 Σ 50

06425607001

REF 790-1015 Σ 250

06425623001

IVD

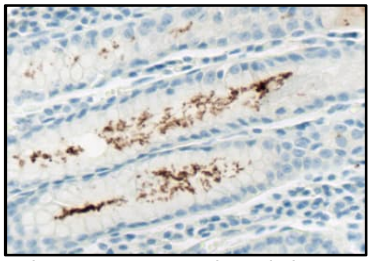

Figure 1. VENTANA anti-H. pylori (SP48) antibody staining of Helicobacter pylori organisms in gastric tissue.

INTENDED USE

VENTANA anti-Helicobacter pylori (SP48) Rabbit Monoclonal Primary Antibody is intended for laboratory use in the qualitative immunohistochemical detection of *Helicobacter pylori* by light microscopy in sections of formalin-fixed, paraffin-embedded gastric biopsy tissue stained on a Benchmark IHC/ISH instrument. Immunohistochemical staining with this antibody product may aid in the diagnosis of *Helicobacter pylori* infection.

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

Helicobacter pylori is a gram-negative bacteria that can colonize the human gastric mucosa and cause the development of peptic ulcers and gastritis.[1,2,3] Long term infection and irritation by the organism results in a specific humoral immunologic response that is thought to lead to gastric carcinogenesis and gastric lymphoma.[1] VENTANA anti-Helicobacter pylori (SP48) Rabbit Monoclonal Primary Antibody (VENTANA anti-H. pylori (SP48) antibody) may aid in the diagnosis of *H. pylori* infection in gastric endoscopic biopsies. The characteristic helical shape and localization of the organisms within the crypts of the mucosa assist the clinician in making an accurate diagnosis of infection, even when very low numbers of organisms are present.[4,5]

PRINCIPLE OF THE PROCEDURE

VENTANA anti-H. pylori (SP48) antibody is a recombinant rabbit monoclonal antibody generated against whole lysate of *Helicobacter pylori* which binds to the organism in formalin-fixed paraffin-embedded (FFPE) tissue sections. The specific antibody can be visualized using *ultra*View Universal DAB Detection Kit (Cat. No. 760-500 / 05269806001). Refer to the *ultra*View Universal DAB Detection Kit method sheet for further information.

MATERIAL PROVIDED

VENTANA anti-H. pylori (SP48) antibody (Cat. No. 790-1014) contains sufficient reagent for 50 tests.

One 5 mL dispenser of VENTANA anti-H. pylori (SP48) antibody contains approximately 27.0 µg of rabbit monoclonal antibody.

VENTANA anti-H. pylori (SP48) antibody (Cat. No. 790-1015) contains sufficient reagent for 250 tests.

One 25 mL dispenser of VENTANA anti-H. pylori (SP48) antibody contains approximately 135.0 µg of rabbit 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 5.4 µg/mL.

VENTANA anti-H. pylori (SP48) antibody is a recombinant rabbit monoclonal antibody generated using a whole lysate of the *H. pylori* bacteria.

Refer to the *ultra*View Universal DAB 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. Rabbit Monoclonal Negative Control Ig (Cat. No. 790-4795 / 06683380001)
4. *ultra*View Universal DAB Detection Kit (Cat. No. 760-500 / 05269806001)
5. EZ Prep Concentrate (10X) (Cat. No. 950-102 / 05279771001)
6. Reaction Buffer Concentrate (10X) (Cat. No. 950-300 / 05353955001)
7. LCS (Predilute) (Cat. No. 650-010 / 05264839001)
8. ULTRA LCS (Predilute) (Cat. No. 650-210 / 05424534001)
9. Cell Conditioning Solution (CC1) (Cat. No. 950-124 / 05279801001)
10. ULTRA Cell Conditioning Solution (ULTRA CC1) (Cat. No. 950-224 / 05424569001)
11. Hematoxylin II (Cat. No. 790-2208 / 05277965001)
12. Bluing Reagent (Cat. No. 760-2037 / 05266769001)
13. Permanent mounting medium
14. Cover glass
15. Automated coverslipper
16. General purpose laboratory equipment
17. 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.[6] 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.

The use of Superfrost® Plus slides, or equivalent, is recommended.

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. Do not use beyond the specified number of tests.
4. 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.
5. 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.

6. 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.[7,8]
7. Avoid contact of reagents with eyes and mucous membranes. If reagents come in contact with sensitive areas, wash with copious amounts of water.
8. Avoid microbial contamination of reagents as it may cause incorrect results.
9. 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 navifyportal.roche.com.
10. Consult local and/or state authorities with regard to recommended method of disposal.
11. Product safety labeling primarily follows EU GHS guidance. Safety data sheet available for professional user on request.
12. 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

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 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 790-1014 or 790-1015.

Table 2. Recommended staining protocol for VENTANA anti-H. pylori (SP48) antibody with *ultra*View Universal DAB Detection Kit on BenchMark IHC/ISH instruments.

Procedure Type	Method	
	XT	ULTRA or ULTRA PLUS
Deparaffinization	Selected	Selected
Cell Conditioning (Antigen Unmasking)	CC1, Standard	ULTRA CC1, Standard
Antibody (Primary) Select anti-H.pylori [4374]	16 minutes, 37°C	16 minutes, 36°C
Counterstain	Hematoxylin II, 4 minutes	
Post Counterstain	Bluing Reagent, 4 minutes	

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."[9]

NEGATIVE REAGENT CONTROL

In addition to staining with VENTANA anti-H. pylori (SP48) antibody, a second slide should be stained with Rabbit Monoclonal Negative Control Ig.

POSITIVE TISSUE CONTROL

Optimal laboratory practice is to include a positive control section on the same slide as the test tissue. This helps identify any 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. Control tissue should be fresh autopsy, biopsy, or surgical specimen, prepared or fixed as soon as possible in a manner identical to test sections.

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

H. pylori positive gastric tissue should be used as a positive control tissue for this antibody. For the test to be considered valid, the positive control tissue should exhibit staining of Helicobacter pylori organisms. Tissue with known negative *H. pylori* status can be used as a negative tissue control. This negative tissue control should be stained with VENTANA anti-H. pylori (SP48) antibody to ensure that the antigen enhancement and other pretreatment procedures did not create false positive staining.

STAINING INTERPRETATION / EXPECTED RESULTS

VENTANA anti-H. pylori (SP48) antibody stains the entire *Helicobacter pylori* organism. The *Helicobacter pylori* organisms when stained by IHC commonly appear as dark brown to black helical, comma, seagull, or S-shaped bodies, approximately 3 µm long in the epithelial or luminal surface of the gastric mucosa. The organisms may also be observed in the deeper crypts of heavily infected gastric samples. Atypical coccoid (encysted) forms may also be seen, especially if a patient has undergone previous antibiotic therapy. The size, shape and location of organism staining is important to note because staining in a pattern or location different from the one described above may suggest non-specific staining or cross-reactivity.

Proper use of the *ultra*View Universal DAB Detection Kit results in a dark brown colored precipitate at the site of specific antibody binding. A qualified pathologist who is experienced in immunohistochemical 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.

Refer to recommendations for staining interpretation listed below in Table 3.

Table 3. Definition of *Helicobacter pylori* detection using VENTANA anti-H. pylori (SP48) antibody.

Definition of *H. pylori* Detected	Definition of *H. pylori* Not Detected
The stain allows for one or more organisms to be visualized and the size, morphology and location of the stained organism is consistent with that of *H. pylori*.	No organisms are stained, or organism stained is not consistent with appropriate size and morphology of *H. pylori*.

SPECIFIC LIMITATIONS

VENTANA anti-H. pylori (SP48) antibody was not challenged with *Campylobacter coli*, *Campylobacter fetus*, *Borrelia burgdorferi*, *Yersinia enterocolitica*, *Proteus mirabilis* and *Pseudomonas aeruginosa*, therefore the performance with these organisms is unknown.

This antibody has been optimized for use on BenchMark IHC/ISH instruments in combination with *ultra*View Universal DAB Detection Kit but the user must validate results obtained with this reagent. This antibody demonstrated a cross-reactivity with the *Campylobacter jejuni* organism, but no cross-reactivity with any other enteric bacteria was noted.

Cross-reactivity of VENTANA anti-H. pylori (SP48) antibody to microorganisms was determined by testing FFPE samples of aspergillus, *Pneumocystis carinii*, *spirochetes*, *Cryptococcus neoformans*, and *mycobacterium*. Testing was also completed on cytospins of *Campylobacter jejuni* and *Escherichia coli*. Negative staining was obtained on *aspergillus*, *Pneumocystis carinii*, *spirochetes*, *Cryptococcus neoformans*, *mycobacterium*, and *Escherichia coli*.

PERFORMANCE CHARACTERISTICS

ANALYTICAL PERFORMANCE

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

Specificity and Sensitivity

Table 4. Specificity/Sensitivity of VENTANA anti-H. pylori (SP48) antibody was determined by testing FFPE normal tissues.

Tissue	# positive / total cases	Tissue	# positive / total cases
Cerebrum	0/3	Esophagus	0/3
Cerebellum	0/3	Stomach	2/3
Adrenal gland	0/3	Small intestine	0/3
Ovary	0/3	Colon	0/3
Pancreas	0/3	Liver	0/3
Lymph node	0/3	Salivary gland	0/3
Pituitary gland	0/3	Kidney	0/3
Testis	0/3	Prostate	0/3
Thyroid	0/3	Bladder	0/3
Breast	0/3	Parathyroid gland	0/3
Spleen	0/3	Endometrium	0/3
Tonsil	0/3	Cervix	0/3
Thymus	0/3	Skeletal muscle	0/3
Bone marrow	0/3	Skin	0/3
Lung	0/3	Nerve	0/3
Heart	0/3	Mesothelium	0/3

Table 5. Specificity/Sensitivity of VENTANA anti-H. pylori (SP48) 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 adenocarcinoma (Ovary)	0/1
Adenocarcinoma (Ovary)	0/1
Neuroendocrine neoplasm (Pancreas)	0/1
Adenocarcinoma (Pancreas)	0/1
Seminoma (Testis)	0/1
Embryonal carcinoma (Testis)	0/1
Medullary carcinoma (Thyroid)	0/1
Microinvasive ductal carcinoma (Breast)	0/1
Ductal carcinoma in situ (Breast)	0/1
Invasive ductal carcinoma (Breast)	0/1
B-cell Lymphoma, NOS (Spleen)	0/1
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 (Small Intestine)	0/1
Adenocarcinoma (Colon)	0/1
Gastrointestinal stromal tumor (Colon)	0/1
Adenocarcinoma (Rectum)	0/1
Gastrointestinal stromal tumor (Rectum)	0/1
Hepatocellular carcinoma (Liver)	0/1
Hepatoblastoma (Liver)	0/1
Clear cell carcinoma (Kidney)	0/1
Adenocarcinoma (Prostate)	0/2
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
Neuroblastoma (Retroperitoneum)	0/1
Mesothelioma (Peritoneum)	0/1

Pathology	# positive / total cases
B-Cell Lymphoma, NOS (Lymph node)	0/2
Hodgkin lymphoma (Lymph node)	0/1
Urothelial carcinoma (Bladder)	0/1
Leiomyosarcoma (Bladder)	0/1
Spindle cell rhabdomyosarcoma (Peritoneum)	0/1
Leiomyosarcoma (Smooth muscle)	0/1

Precision

Single-site precision studies for VENTANA anti-H. pylori (SP48) antibody included the following testing:

1. Between-lot precision was determined by testing 3 antibody lots across triplicate slides of 24 gastric tissues (12 positive, and 12 negative for *H. pylori*) on a BenchMark XT instrument. Between-lot precision was 100%.
2. Between-run intermediate precision was determined by staining duplicate slides of 24 gastric tissues (12 positive, and 12 negative for *H. pylori*) on a BenchMark XT instrument over 5 non-consecutive days over at least a 20 day period. Between-run intermediate precision was 100%.
3. Within-run intermediate precision was determined by staining 24 gastric tissues (12 positive, and 12 negative for *H. pylori*) across 5 slides on a BenchMark XT instrument. Within-run intermediate precision was 100%.
4. Between-instrument intermediate precision was determined on the BenchMark XT instrument by staining duplicate slides of 24 gastric tissues (12 positive, and 12 negative for *H. pylori*) on 3 BenchMark XT instruments. Between-instrument intermediate precision on the BenchMark XT instrument was 100%.
5. Between-instrument intermediate precision was determined on the BenchMark ULTRA instrument by staining duplicate slides of 24 gastric tissues (12 positive, and 12 negative for *H. pylori*) on 3 BenchMark ULTRA instruments. Between-instrument intermediate precision on the BenchMark ULTRA instrument was 100%.
6. Between-platform intermediate precision was determined by staining duplicate slides of 24 gastric tissues (12 positive, and 12 negative for *H. pylori*) on 3 BenchMark XT instruments and 3 BenchMark ULTRA instruments. Between-platform intermediate precision across the BenchMark XT and BenchMark ULTRA instruments was 100%.
7. Within-run intermediate precision was determined by staining 24 gastric tissues (12 positive, and 12 negative for *H. pylori*) across 5 slides on a BenchMark ULTRA PLUS instrument. Within-run repeatability was 100%.
8. Between-run intermediate precision was determined by staining duplicate slides of 24 gastric tissues (12 positive, and 12 negative for *H. pylori*) on a BenchMark ULTRA PLUS instrument on 5 non-consecutive days over at least a 20 day period. Between-day intermediate precision was 99.5%.
9. Between-instrument intermediate precision was determined on a BenchMark ULTRA PLUS instrument by staining duplicate slides of 24 gastric tissues (12 positive, and 12 negative for H. pylori) on 3 BenchMark ULTRA PLUS instruments. Between-instrument intermediate precision was 100%.

Multi-site precision studies (Between-site, Between-run, Between-platform, and Between-observer precision) for VENTANA anti-H. pylori (SP48) antibody included the following testing:

Three clinical sites participated in the study. Fourteen FFPE human gastric biopsy specimens were prepared by cutting serial sections of each case and mounting the sections onto glass microscope slides. Three sites stained the same 14 cases, distributed across the three clinical categories (high positive, low positive, negative), using BenchMark ULTRA and BenchMark XT instruments. Each site conducted two staining runs per day, one on the BenchMark XT instrument and one on the BenchMark ULTRA instrument, on each of three non-consecutive days over a minimum of 12 days. Each staining run included all 14 cases. At each site, readers were blinded as to case ID, run number, staining instrument, and *H. pylori* status. The between-site, between-run, and between-reader positive and negative agreement rates for the assay were all 100% on both the BenchMark ULTRA and the BenchMark XT instruments. The morphology and background acceptance rates were also 100% on both the BenchMark ULTRA and the BenchMark XT instruments.

All studies met their acceptance criteria.

Comparison of BenchMark ULTRA Instrument versus BenchMark ULTRA PLUS Instrument

A study was conducted to compare the staining performance of the VENTANA anti-H. pylori (SP48) antibody on the BenchMark ULTRA PLUS instrument versus the BenchMark ULTRA instrument. One hundred twenty (120) gastric or small intestine tissue cases (60 positive for *H. pylori* and 60 negative for *H. pylori*) were stained, and the stained slides were evaluated by a pathologist who determined the diagnostic status.

Table 6. VENTANA anti-H. pylori (SP48) antibody on the BenchMark ULTRA PLUS instrument and VENTANA anti-H. pylori (SP48) antibody on the BenchMark ULTRA instrument.

BenchMark ULTRA PLUS instrument	BenchMark ULTRA instrument		
	Positive	Negative	Total
Positive	52	1	53
Negative	3	51	54
Total	55	52	107
	n/N	% (95% CI)	
Positive percent agreement	52/55	94.5 (85.1-98.1)	
Negative percent agreement	51/52	98.1 (89.9-99.7)	
Overall percent agreement	103/107	96.3 (90.8-98.5)	

The morphology acceptability rate for all slides stained in this study was 100.0% (95% C.I. 96.6%-100.0%) for the BenchMark ULTRA PLUS instrument. The background acceptability rate was 100.0% (95% C.I. 96.6%-100.0%) for the BenchMark ULTRA PLUS instrument.

CLINICAL PERFORMANCE

Performance of the assay was established in preclinical studies comparing detection of *H. pylori* with VENTANA anti-H. pylori (SP48) antibody to a modified Giemsa assay in human gastric tissue samples that ranged from not colonized to heavily colonized with *H. pylori*. *H. pylori* status was scored as not detected, detected, or not evaluable.

A retrospective method comparison study was conducted at three independent clinical sites to evaluate the positive and negative percent agreement rates between VENTANA anti-H. pylori (SP48) antibody and the Giemsa Staining Kit (Cat. No. 860-006 / 05279224001) in determining the presence of *H. pylori in gastric biopsy tissue*.

The three sites targeted acquisition of a total of 300 *H. pylori* samples, actually stained 299 cases, and obtained complete data on 294. Samples were excluded for H&E non-acceptability (1), Giemsa slide tissue morphology non-acceptability (2), Giemsa slide tissue morphology and VENTANA anti-H. pylori (SP48) antibody slide tissue morphology non-acceptability (3), and VENTANA anti-H. pylori (SP48) antibody negative control stain not negative.

Each site prepared seven slides per case by freshly cutting serial sections of tissue of 3 micron thickness from archived FFPE tissue blocks and mounting sections in the same direction on each slide. Samples for the study were identified at the clinical study sites via pre-screening based on consecutive cases where *H. pylori* was detected or not detected based on patient medical records of the results from evaluation of gastric biopsies. Investigators at each site for the method comparison analysis of the investigational device and the comparator device were blinded to *H. pylori* status of each specimen and slides were read in the order in which they were provided. The ages of the FFPE tissue blocks that were included in the clinical study ranged from 11-666 days.

Pooled data from all sites demonstrated a slide staining acceptability rate for slide background in 298/299 human gastric biopsy tissue samples stained with VENTANA anti-H. pylori (SP48) antibody. Pooled data from all sites demonstrated a slide staining acceptability rate for slide tissue morphology in 298/299 human gastric biopsy tissue samples stained with VENTANA anti-H. pylori (SP48) antibody.

Table 7. Agreement Data: VENTANA anti-H. pylori (SP48) antibody and Giemsa Staining Kit.

VENTANA anti-H. pylori (SP48) antibody	Giemsa Stain		
	Detected	Not Detected	Not Available
Detected	136	2	1
Not Detected	3	153	1
Not Evaluable	1	1	1

Positive Percent Agreement = 97.8% (93.8% - 99.3%)

Negative Percent Agreement = 98.7% (95.4% - 99.6%)

Pooled data from all sites demonstrated positive agreement in 136/139 human gastric biopsy tissue samples and negative agreement in 153/155 human gastric biopsy tissue samples between VENTANA anti-H. pylori (SP48) antibody and the Giemsa Staining Kit. These numbers translate into a positive percent agreement of 97.8%, with a 95% confidence interval of (93.8- 99.3); the negative percent agreement was 98.7%, with a 95% confidence interval of (95.4- 99.6).

Pooled data from all sites demonstrated positive agreement in 138/151 human gastric biopsy tissue samples, and negative agreement in 144/145 human gastric biopsy tissue samples between VENTANA anti-H. pylori (SP48) antibody and the *H. pylori* diagnosis obtained from the enrollment pathology reports. These numbers translate into a positive percent agreement of 91.3%, with a 95% confidence interval of (85.7- 95.3); the negative percent agreement was 99.3%, with a 95% confidence interval of (96.2- 99.9).

REFERENCES

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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 elabdoc.roche.com/symbols for more information).

GTIN	Global Trade Item Number
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

REVISION HISTORY

Rev	Updates
F	Updates to Warnings and Precaution section. Updated to current template.

INTELLECTUAL PROPERTY

For USA: Rx only

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