OnSite™
H. Pylori Ag Rapid Test

A lateral flow immunoassay for the qualitative detection of Helicobacter pylori (H. pylori) Antigen in human fecal specimens

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Section A) PRODUCT DESCRIPTION

1. Product Description

The *OnSite* H. Pylori Ag Rapid Test is a lateral flow chromatographic immunoassay for the qualitative detection of *H. pylori* antigen in human fecal specimen. It is intended to be used by professionals as a screening test and provides a preliminary test result to aid in the diagnosis of infection with *H. pylori*. Any interpretation or use of this preliminary test result must also rely on other clinical findings as well as on the professional judgment of health care providers. Alternative test method(s) should be considered to confirm the test result obtained by this device.

2. Intended Use

The *OnSite* H. Pylori Ag Rapid Test is intended to be used as a screening test and provides a preliminary test result to aid in the diagnosis of infection with *H. pylori*.

3. Device Classification

- USA: Class II device
- Europe: Annex III Other
- India: Non–critical device

Section B) TECHNICAL REQUIREMENTS

1. General Requirements Checklist

General requirements		Apply	Applied Standards	Demonstrated By:	Location:
1.	Safe use for Patient, User, Environments	Yes	EN ISO 14971 : 2012	Risk Management File	Attachment # 1
2.	Solutions To Ensure Safety, Including Elimination/ reduction of risk, Taking Appropriate Action when appropriate and informing users of residual risk	Yes	EN ISO 14971 : 2012	Risk Management File	Attachment # 1
3	They are suitable for the purposes referred to in Article 1(2)(b), & meet manufacturer stated Performance Expectations	Yes	EN 13612 : 2002	IFU & Product Performance	Attachment # 2 & Attachment # 4
4.	Product Safety and Performance must not be affected during product lifetime when exposed to normal stresses and conditions	Yes	EN ISO 23640 : 2013	Stability Study	Attachment #5
5.	Devices designed and manufactured so that performance is not adversely affected under storage and transport conditions.	Yes	EN ISO 23640 : 2013	Pouch Package Study	Attachment # 9
6.	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 2: In vitro diagnostic reagents for professional use (ISO 18113-2:2009)	Yes	EN ISO 18113-2:2009	IFU	Attachment # 2
7.	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 1: Terms, definitions and general requirements	Yes	EN ISO 181131:2009	IFU	Attachment # 2
8.	Sampling procedures used for acceptance testing of in vitro diagnostic medical devices - Statistical aspects	Yes	EN ISO 13975: 2003	Sampling and acceptance procedure	SOP-82-04 and WI 82-04-1

2. Design and Manufacturing Requirements

Design and Manufacturing Requirements		Apply	Standards	Demonstrated By:	Location:
1	**CHEMICAL AND PHYSICAL PROPERTIES**				
1.1	Device characteristics and performance in relation with intended use	Yes	EN 13612 : 2002	Product Performance	Attachment #4
1.2	Risks posed by device leakage, contaminants and residues	Yes	EN ISO 14971 : 2012 EN 13641: 2002	MSDS	Attachment # 8
2	**INFECTION AND MICROBIAL CONTAMINATION**				
2.1	Reduction of the risk of infection and/or contamination	Yes	EN ISO 14971 : 2012 EN 13641:2002	Risk Management, MSDS, IFU	Attachment #1, #2 & # 8
2.2	Reduce risk of biological substances	Yes	EN ISO 14971 : 2012 EN 13641:2002	Risk Management, MSDS, IFU	Attachment #1, #2 & # 8
2.3-2.6	N/A	No	N/A	N/A	N/A
2.7	Packaging	Yes	EN ISO 14971 : 2012 EN 13640:2002	Pouch Package Study	Attachment # 9
3	**MANUFACTURING AND ENVIORNMENTAL PROPERTIES**				
3.1	Tests when connected with other devices and/or accessories	No	N/A	N/A	N/A
3.2	Contact with device materials	No	N/A	N/A	N/A
3.3	Remove risk due to outside influence. (ex. Humidity, temperature)	Yes	EN ISO 14971 : 2012 EN 13640:2002	Risk Management Stability study	Attachment # 1 & Attachment #5
3.4	Flammability	No	N/A	N/A	N/A
3.5	Safe Waste Disposal	Yes	EN ISO 14971 : 2012 EN 13640:2002	IFU, MSDS	Attachment # 2 & Attachment #8
3.6	Ergonomics	No	N/A	N/A	N/A
4-7		**No**	**N/A**	**N/A**	**N/A**
8	**MANUFACTURER INFORMATION**				
8.1	Information for use	Yes	EN1041 : 2008 EN ISO 18113 : 2011 EN ISO 15223-1:2012	Labels, IFU	Section 4.2 & Attachment #2
8.2	Standard Symbol	Yes	EN ISO 15223-1 : 2012	Labels, IFU	Section 4.2
8.3	Danger Symbol	Yes	EN ISO 15223-1 : 2012	Labels	Section 4.2
8.4	Proper Label Format	Yes	EN ISO 15223-1 : 2012	Labels	Section 4.2
8.5	Intended Purpose	Yes	EN 1041 : 2008	IFU	Attachment# 2
8.6	Device and Component Identification	Yes	EN ISO 15223-1 : 2012	Labels	Section 4.2
8.7	Instructions for use	Yes	EN 1041 : 2008 EN ISO 18113:2011	IFU	Attachment # 2

3. RISK ANALYSIS

See Attachment 1: Non-Critical Disease Rapid Test Risk Management Report
The Risk of this product is negligible and no further action needs to be taken.

4. LABELS & INSTRUCTIONS FOR USE

4.1) Instructions for Use: See Attachment 2: I.F.U.

4.2) Direct Labeling of Product

See attached labeling

5. MATERIALS SPECIFICATIONS

5.1) Material Specification

Materials		Specification
Test strip	Overall	64 ± 0.5 mm x 3.5 ± 0.3 mm with five subcomponents
	a. Sample pad	31 ± 1.5 mm x 3.5 ± 0.3 mm Absorb water within 1 second
	b. Conjugate pad	4-5 mm x 3.5 ± 0.3 mm containing anti-*H. pylori* Antibody-colored particle conjugate
	c. Nitrocellulose membrane	20 ± 0.5 mm x 3.5 ± 0.3 mm, Flow rate: 4cm / 110 - 165 seconds backing spotted with *H. pylori* Antibody (T line), and control reagent (C line).
	d. Absorbent pad	15 ± 0.7 mm x 3.5 ± 0.3 mm
	e. Vinyl matte adhesive	64 ± 3.3 mm x 3.5 ± 0.3 mm Pass flow rate test at 45 °C for 7 days
Anti-H. pylori Antibody 1		Purified antibody
Anti-H. pylori Antibody 2		Purified antibody
Colored particle		Standard colored particles
Conjugate pad fabric		Standard pad fabric
Plastic Cassette		72 ± 4.1 mm x 20 ±1 mm A sample receiving well labeled S The position of the T and C lines are marked on the cassette Strip groove fits 3.5 mm x 64 mm strip Pass flow rate test with specimens
Pouch		120 ± 0.6 mm x 65 ± 3.2 mm size with 3-5 mm sealing margin One side is printed with company information and test type. The other side is blank for labeling of production information. No dirty spots Pass 3 day integrity of seal test
Desiccant		0.5 ± 0.1 g
Package Insert		Off white or white paper, 70g A4 paper, left and right margin: 0.5 -1.0 cm; top and bottom margin: 1.0-1.5 cm. Correct art work, color printing, no dirty spots

5.2) Product Specifications

See Attachment 3: Product Specification

5.3) Component Specifications

5.3.1) Test Characteristic

Nitrocellulose-based membrane strip with a T line pre-coated with unconjugated *H. pylori* antibody, a C line pre-coated with a control line antibody, and a conjugate pad containing colored particles conjugated anti-*H. pylori* antibody.

5.3.2) Kit composition and specifications

Kit Composition

Composition	Specification
1. Device	25 single use devices in each kit. Each is individually sealed, and contains two items inside: 1. One cassette device composed of a test strip and a plastic housing cassette 2. One desiccant: 0.5 g
2. Plastic dropper	10 plastic droppers in each kit for watery fecal specimens
3. Stool Collection Device	25 devices in each kit 1 mL Extraction Buffer in each bottle
4. Package insert	One insert each kit

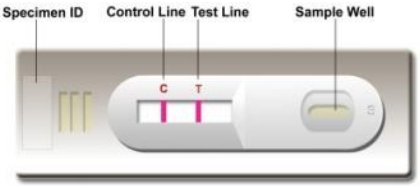
Kit Box

Specification	Dimension	Capacity
CTK H. Pylori Ag Specific (PM-R0192C)	12.4 cm (W) x 22.2 cm (L) x 7.05 cm (H)	25 test devices

5.3.3) Test Appearance

The *Onsite* H. Pylori Ag Rapid Test is a cassette device. The device has following letters on the surface of the cassette:

T: Test Line Position
C: Control Line Position
S: Sample Well



Both the Test line and the Control line in the result window are not visible before applying any samples.

If a positive specimen is applied, both the Test line and Control line will appear.

If a negative specimen is applied only the C line will appear. The Control line is used for procedural control. The Control line should always appear if the procedure is performed properly and the test reagents are working.

6. CLINICAL STUDIES & PERFORMANCE EVALUATIONS

See Attachment 4: Product Performance

7. STABILITY STUDIES

See Attachment 5: Stability Study

8. MANUFACTURING

8.1) Manufacturing Process

The entire manufacturing process has seven sequential process steps and is jointly accomplished by seven production groups

Step #1 **Conjugate anti-*H. pylori* with colored particles and preparation of conjugation pad**

- Preparation of colored particle solution.
- Add conjugation buffer, then add anti-*H. pylori* antibody to the solution
- Add blocker,
- Centrifuge
- Collect conjugate
- Dissolve the conjugate with conjugate suspension buffer
- Dispense the conjugates to the conjugate pad material
- Dry the conjugate pad

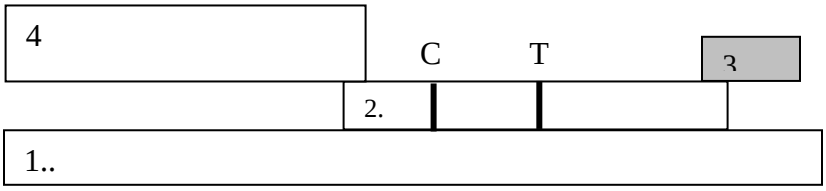
Step #2 **Coat T and C line on the NC membrane**

- Preparation of membrane lamination: Fix a 20 mm x 300 mm of nitrocellulose membrane onto the 300 mm x 66 mm of vinyl matte adhesive.
- Prepare the T line and C line coating solutions.
- Dispense the reagents to the T and C positions on the membrane with the coating machine (sprayer)
- The coated membrane is then dried

Step #3 **Lamination**

- Assemble all the components to sheet according to scheme illustrated below
- Laminate the components according to scheme illustrated below
- QC samples the uncut sheet with the QC positive detection, specificity, and limit of detection panels.

[Cross Section Scheme of Lamination]



1. Vinyl matte adhesive
2. NC membrane coated with T and C line.
3. Conjugate pad
4. Absorbent pad

Step #4 **Cutting**

- Laminated sheets are cut into the size of 3.5 mm x 68 mm.
- The size of the strip is inspected at the beginning, middle and end of the run.

Step #5 **Cassette Assembling and Sealing**

- Pouch is labeled with name, mfg date, exp. date, and catalog, according to the documentation
- Assemble the cut strip into the plastic housing cassette and press to close the cassette
- Pack one cassette and one desiccant to each pouch
- Seal the pouch with the heat sealing machine
- Inspect packing process by reconciliation of the quantity of components picked, the quantity of pouch assembled, and the quantity of unused components.

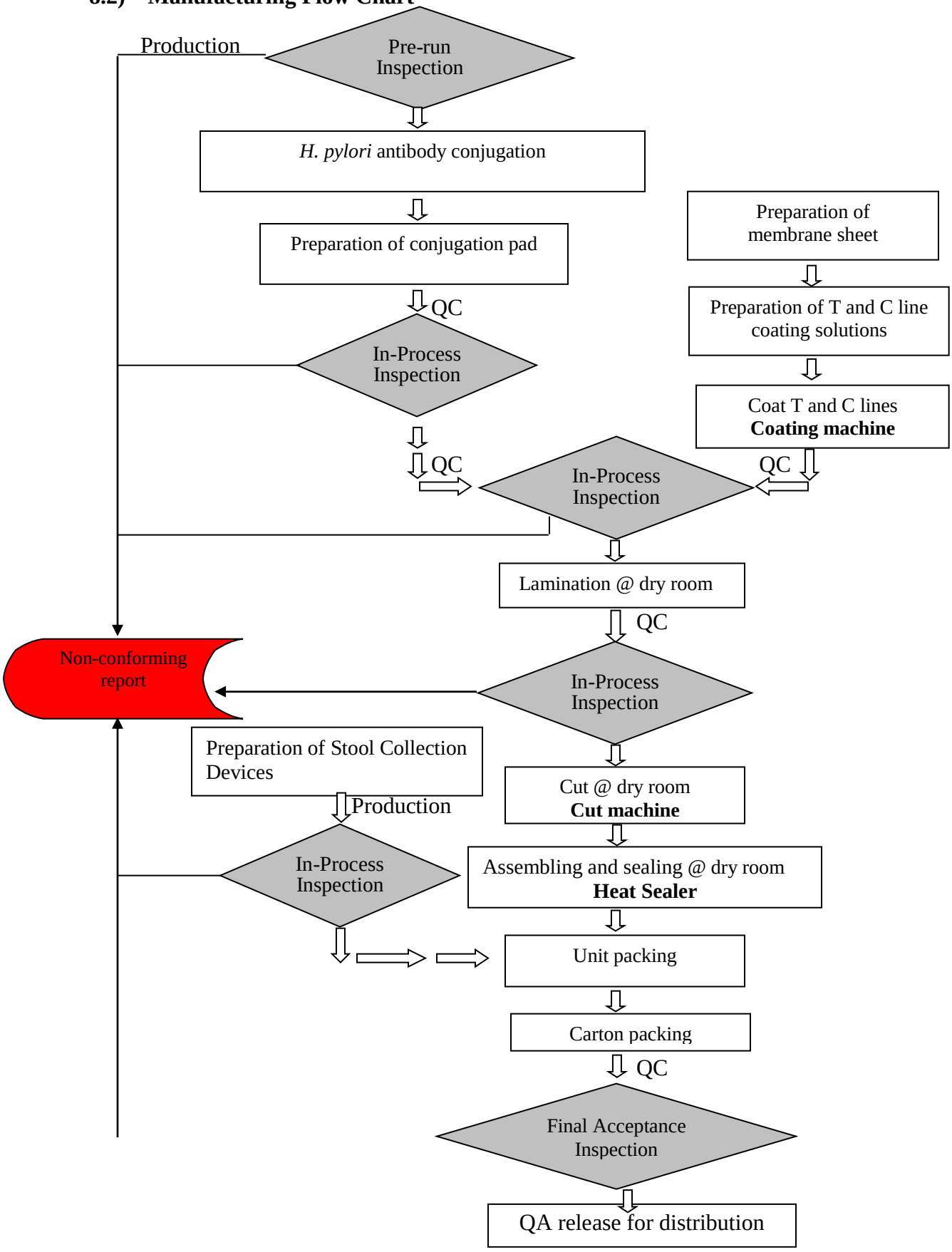
Step #6 **Preparation of Sample Extraction Buffer**

- Prepare Sample Extraction Buffer according to formulation
- Aliquot 1 mL into each extraction tube
- Ensure all bottles are properly labeled
- Inspect all the bottles for leakage at 2 Psi for 2 minutes.

Step #7 **Unit Packing**

- Pick up all required components (Extraction Buffer, Devices) and labels including package inserts, zip lock bag (bulk package) and kit box
- Pack to unit
- Inspect packing process by reconciliation of the quantity of components picked, the quantity of units packed, and the quantity of unpacked components
- Packed product is moved to the quarantine area awaiting Final Acceptance Inspection

8.2) Manufacturing Flow Chart



8.3) Production Specifications

Production Process	Specification
Pre-run Inspection	Antibody has less than 10% degradation by SDS-PAGE
Colored conjugate solution	Validated process
Conjugation	First run inspection passes QC panel Conjugate pad is uniformly sprayed with conjugates. Dryness of the conjugate pad Conjugate pad passes test with QC panel
Coating	The dispensing volume is calibrated at the start of the process by checking the accuracy of the volumes dispensed. T and C lines are coated at designated area and inspected at the start run, middle run, and final run. Dryness of the membrane Coated membrane passes test with QC panel
Lamination	First run inspection passes test with QC panel All the components are laminated correctly by visual inspection according to Inspection Sample Plan.
Cutting	3.5 $\pm$ 0.1 mm wide each strip verified by inspection at start of run, middle-run, and final run.
Cassette assembling and pouching	All the strips are properly assembled into the cassettes by visual inspection during processing. All the pouches are labeled correctly by visual inspection All the components are packed correctly by reconciliation of the quantity of the components picked and used.
Preparation of Sample Extraction Buffer	Solution is made with the correct formulation. Fill in volume 1 mL $\pm$ 0.1 mL based on the sampling plan No leaking upon test inspection.
Unit Packing	All the components are packed correctly by reconciliation of the quantity of the components picked and packed.

8.4) Documentation of Quality System

This product is manufactured in a facility certified to be in accordance with the ISO 13485 Quality System

See Attachment 6: ISO Certification

9.) BATCH RELEASE CRITERIA

Quality Control Inspection and Specifications:
Quality control inspection is performed on all raw materials and intermediate components produced, as well as the assembled kits. The inspection of the product is based on the following protocols:

9.1) Incoming Material Inspection

Incoming Material Inspections are performed on all in-coming raw materials. The quarantined raw materials are sampled per Inspection Sample Plan by QC department for inspection per specification described at section 5.1
Upon inspection, the QC supervisor will endorse the inspection data and assign quality status to the raw materials accordingly.
Only approved raw materials are used for production of product.

9.2) In-Process Inspection

All lots of individual intermediate components produced are inspected and tested during the process. A systematic sampling of each individual lot of intermediate components is taken for In-Process Inspection per specification described at section 5.1
Function tests are performed by assaying the intermediate components with the QC control panel, and with a reference intermediate component on the *OnSite* H. Pylori Ag Rapid Test if necessary. Physical inspections of the test components, such as the fill volume, appearance, and physical status are also carried out.
Upon analyzing the inspection results, the QC supervisor will assign the quality status of the intermediate components. The approved intermediate components are moved from the quarantined storage area to the approved storage area. Components that do not pass inspection will be rejected and not used in production.

9.3) Final Acceptance Inspection

Final acceptance inspection is carried out once all the components are assembled into the final packing unit. The inspection is to ensure only the product that meets the specification is released for distribution. The inspection includes:

- Document Inspection: Inspection of all production work records
- Physical Inspection: Inspect based on the Sampling Plan. The inspection includes checking the labels, lot number and expiration date of the individual components as well as the assembled kit. Inspection is also performed to ensure that all the components are packed.
- Performance Inspection: At least 40 tests submitted by the Production group are inspected with four *OnSite* H. Pylori Ag Rapid Test QC control panels. The panels consist of 6 members of a positive detection panel, 20 members of a specificity panel, 1 or 2 member of a precision panel and 3 members of limit of detection panel for testing product's positive detection, specificity, precision and limit of detection.

- Kits are ready for shipment once they have passed this final stage of QC inspection.
- QA will endorse the release of the product and retain at least 40 tests for future analysis.

9.4) Procedure of the Final Acceptance Inspection

Introduction
Each kit of *Onsite* H. Pylori Ag Rapid Test (R0192C) contains the following components:

a. 25 test devices, each sealed in a foil pouch with two items inside:
   - One cassette device
   - One desiccant

b. 10 plastic droppers for watery fecal specimen
c. 25 Stool Collection Devices
d. One package insert (instruction for use)

Quality control evaluation is performed on every lot of these components.

Inspection Procedures:
The quality control procedures used for evaluation of the finished products are:

a. Physical Inspection
   According to the Inspection Sample Plan, obtain the required quantity of tests, inspect following parameters:
   - Content in each package: Make sure each pack contains the correct quantity of components
   - Labels: Make sure all labels correspond to documentation
   - Pouch Integrity: Make sure the pouch is sealed properly
   - Pouch Content: Open pouch to check contents. Make sure all the contents are included.
   - Stool Collection Device Integrity: Make sure no leakage is visible

   Record the number of the defects observed. Refer to the Acceptance Number (Ac). Pass inspection if the number (Ac) is less than the maximum allowable defects or defectives in a sample for the lot to be accepted based on the sampling plan.

b. Performance Inspection
   Each lot of the *Onsite H. Pylori* Ag Rapid Test is inspected for its positive detection, specificity, precision and limit of detection.

   - Positive detection Inspection
     - Inspection is carried with the *OnSite* H. Pylori Ag Rapid Test Positive detection QC panel. The panel consists of 6 members, numbered SM-R0192-P1 to P11.
     - The assay is performed and interpreted using the procedure described in

the Product Insert.
- Each member specimen is assayed in duplicate.

▪ Specificity Inspection
- Inspection is carried with the *OnSite* H. Pylori Ag Rapid Test Specificity QC panel. The panel consists of 20 members, numbered SM-R0192-N1 to N20.
- The assay is performed and interpreted using the procedure describedin the Product Insert

▪ Precision Inspection
- Inspection is carried out with *OnSite* H. Pylori Ag Rapid Test Precision panel consisting of one weak positive and one medium positive sample.
- The assay is performed and interpreted using the procedure described in the Product Insert.
- Each sample is assayed in 10 replicates. Total of 10 Devices are used for the inspection.
- The flow rate of each device is recorded during the inspection.

▪ Limit of Detection (LOD)
- Inspection is carried out with the 3 members of the LOD Panel.
- Each member specimen is assayed in duplicate.
- The assay is performed and interpreted using the procedure described in the Product Insert.

c. Acceptance Criteria

▪ The Positive detection Inspection result must meet the specification indicated in the following table.

H. Pylori Ag Positive Detection Panel	Sample (N)	Result
SM-R0192-P1~P11	11	All Positive

▪ The Specificity result must meet the specification indicated in the following table.

H. Pylori Ag Specificity Panel	Sample (N)	Result
SM-R0192-N1~N20	20	100% Negative

▪ The Precision Inspection result must meet the specification indicated in the following table.

H. Pylori Ag Precision Panel	Runs	Result	Flow Rate
SM-R0192-C- Weak Positive	10	Equivalent test line intensity	migration: < 120 seconds
SM-R0192-C- Medium Positive	10	Equivalent test	migration:

		line intensity	< 120 seconds

The Limit of Detection Inspection result must meet the specification indicated in the following table

H. Pylori Ag Limit of Detection Panel	Result
SM-R0192-L1 (2 ng/mL)	+
SM-R0192-L2 (1 ng/mL)	+
SM-R0192-L3 (0.5 ng/mL)	+ or –

Note: +: Positive; + or –, Positive or negative,

d. Reference Components Used in QC

The reference components used for inspection of individual intermediate components are approved components from previous production lots. These reference components are tested to ensure that results obtained are within the QC specification for the product.

e. See Attachment 7: Certificate of Analysis.

10.) CONCLUSION

The *OnSite* H. Pylori Ag Rapid Test is developed, manufactured, and marketed according to the ISO13485 quality standard. In a study with specimens from 157 patient fecal samples tested on UBT gold standard method and the *OnSite* H. Pylori Ag Rapid Test had a Relative Sensitivity of 97%, a Relative Specificity of 94%, and an Overall Agreement of 95%. The test does not require equipment and can be performed by technicians with minimal training. It can be stored for 24 months at 2-30°C. Thus, the test is deemed acceptable for marketing and sale wherever the regulatory requirement is completed.