

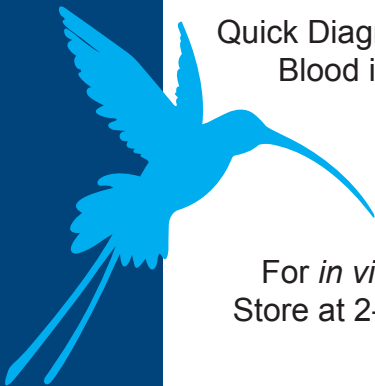
BIOHIT

Innovating for Health

Biohit Oyj

ColonView Hb and Hb/Hp Test (30)

Quick Diagnosis of Fecal Occult
Blood in Stool Samples



For *in vitro* diagnostic use
Store at 2-30°C Upon Receipt

INSTRUCTIONS FOR USE

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REF 602 250

IVD



ColonView Hb and Hb/Hp Test (30) Cat. No. 602 250

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APPENDIX: QUALITY CONTROL CERTIFICATE

1. INTENDED USE

ColonView HB and Hb/Hp Fecal Occult Blood Test is a visual, immunochromatography quick test for the qualitative detection of human hemoglobin (Hb) and hemoglobin/haptoglobin complex (Hb/Hp) in stool samples. The test is intended for professional *in vitro* diagnostic use.

2. CLINICAL BACKGROUND

ColonView Hb and Hb/Hp Fecal Occult Blood Test (FOB) test was designed to aid diagnosis of lower GI pathologies, such as colorectal cancers and large adenomas that bleed. Colorectal cancer is one of the most commonly diagnosed cancers and a leading cause of cancer death in the United States (1-2). Screening for colorectal cancer probably increases the cancer detection at an early stage, therefore reducing the mortality (3-5).

Earlier commercially available FOB tests utilized the guaiac test, which requires special dietary restriction to minimize false positive and false negative results. ColonView Hb and Hb/Hp tests are specially designed to detect human hemoglobin in stool samples using immunochemical methods, which improved specificity for the detection of lower GI disorders, including colorectal cancers and adenomas (6-10).

A molecule of Hb consists of 2 pairs of peptide (alpha and beta globins) chains and four heme groups, each with one atom of iron. Free Hb may separate into alpha-beta molecules, which are bound to a protein called haptoglobin. Hb/Hp complex plays an important role in the retrieval of hemoglobin from lysed erythrocytes and is relatively stable against acid and proteolytic degradation. This means that the Hb/Hp complex can be detected even after longer passages through the bowel. This means that blood mixed with larger intestinal polyps and higher carcinomas can also be detected. Detection of the Hb/Hp complex displays a significant increase in sensitivity with regard to the recognition of colorectal adenomas, and with regard to also carcinomas when combined with Hb detection (8-9).

3. PRINCIPLE OF THE TEST

The ColonView Hb and Hb/Hp Test (30) is based on an immunochromatographic method, in which both Hb and Hb/Hp complexes are specifically recognized through specific antibody reactions.

The Test Cassette strip is pre-coated with anti-human hemoglobin and anti-human haptoglobin antibodies on the Test region (T) and goat anti-mouse antibodies on the Control region (C). An anti-human hemoglobin/haptoglobin complex antibody-colloidal gold conjugate pad is placed at the end of the membrane. When human Hb/Hp complexes are present in the patient stool sample dissolved in buffered saline, the mixture of colloidal gold conjugate and extracted sample moves along the membrane chromatographically by capillary action.

In the case of a positive result, the molecules from the stool sample loaded with gold-marked antibodies attach to the test band (T) and are visible by means of a pink/red coloration. In the case of a negative result, there are no hemoglobin molecules that can attach to the test band (T) as complexes and therefore, there can also be no coloration of the test band (T).

If the control strip (C) turns red/pink in color, this shows that the sample has been taken correctly and has migrated correctly. The test is therefore valid.

4. KIT CONTENTS AND REAGENT PREPARATION

Each ColonView Hb and Hb/Hp Test (30) kit contains reagents for 30 tests. Each test kit contains:

4.1 Test Cassettes

Contents: 30 individually wrapped Test Cassettes.

Preparation: Ready to use.

4.2 ColonView Sample Collection Bags

Contents: 30 ColonView Sample Collection Bags. Each bag contains one Sample Collection Tube, one piece of Stool Collection Paper, and one Instructions for sample collection.

Sample Collection Tube contains 2ml extraction buffer of 0.1 M Tris-HCl buffered saline, with BSA and 0.02% sodium azide.

Preparation: Ready to use

4.3 Instructions for Use

4.4 Quality Control Certificate

5. MATERIALS REQUIRED BUT NOT PROVIDED

A piece of tissue paper to prevent solution from splashing when opening the Sample Collection Tube.

6. STORAGE AND STABILITY

The kit can be stored at 2 ... 30°C until the expiration date.

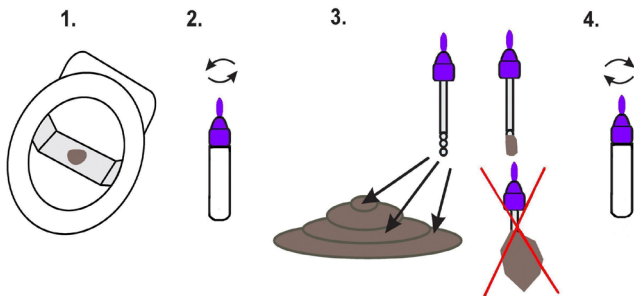
7. WARNINGS AND PRECAUTIONS

- Valid only for in vitro diagnostic use and only for professional use.
- Handle stool specimens as potential biohazardous material.
- It is recommended that the Stool Collection Paper enclosed should be used, in order to avoid mixing with blood from urine samples or interfering components from the toilet water.
- The saline solution in the Sample Collection Tube contains a small amount of sodium azide, which may react with lead or copper plumbing to form potentially explosive metal azides. When disposing of buffered saline or extracted samples, always flush with copious quantities of water to prevent azide build up.
- Do not use the Sample Collection Tube or Test Cassette after the expiration date.
- Only open the Test cassette packaging if the test is actually going to be performed.
- Do not spill solution onto the Test Cassette apart from placing sample into the sample well.
- Patients should follow the instructions for obtaining a sample exactly and should not take any sample during menstruation or in case of bleeding hemorrhoids.
- Bring all reagents to room temperature (20 ... 30 °C) at least 10 minutes before use.
- Evaluate the test result after 5 minutes and not beyond 15 minutes.

8. SAMPLE COLLECTION AND HANDLING

1. Collect a random sample of stool in a clean dry container or receptacle, for example the Stool Collection Paper provided with the Sample Collection Bag. Use the Stool Collection Paper as follows:

- Peel off the liner covering the adhesive tape on each end of the collection paper.
 - Lift toilet seat. Unfold collection paper and place on the rim of toilet bowl. Secure the adhesive tabs on the collection paper to the sides of the toilet rim.
 - Make bowel movement onto collection paper.
2. Unscrew the colored cap and remove the Sample Collection Tube applicator stick. Be careful not to spill or spatter solution from container.
 3. Collect random samples by inserting the applicator stick into the stool specimen. Take samples from various surfaces of the stool specimen.
 4. Re-insert the applicator stick into the tube and screw the cap tightly. Be careful not to break the tip of the Sample Collection Tube (colored end).
 - If you are using the Stool Collection Paper, release adhesive tabs and flush the collection paper with stool.
 5. Write your name and the date of sample collection in the space provided on the Sample Collection Tube.
 6. Return the specimen for testing promptly by mail or in person. The specimen(s) can be stored in the refrigerator (2-8 °C) for no more than 11 days, or at room temperature (max. 25 °C) for no more than 5 days.

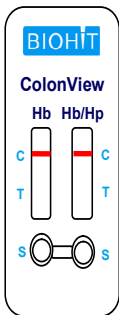


9. TEST PROCEDURE

9.1 Procedure

1. The Test Cassette and the Sample Collection Tube containing the stool sample should be brought to room temperature (20 ... 30°C) at least 10 minutes before testing.
2. Take the required number of Test Cassettes from the foil packaging only immediately before performing the test. Mark the Test Cassette with the name of the patient or with another form of identification.
3. Carefully shake the Sample Collection Tube to ensure that the stool sample mixes properly with the saline solution.
4. Take a paper towel and break the seal of the Sample Collection Tube with rotary motion or use a pair of scissors to cut the seal. Hold the collection tube upright and add 3 drops of the solution into both round sample windows (S) of the Test Cassette.
5. Read the results after 5 minutes. Strongly positive results may be evaluated even sooner. Evaluate the result a maximum of 15 minutes after adding the solution into the round sample windows.

9.2 Quality Control or Internal Procedural Control



The test contains a procedural control. A colored line that appears in the control region (C) shows that each test is performed correctly. It is easy for the background to become slightly yellowish in color during testing, depending on the color of the stool sample. This is acceptable, as long as evaluation of the test results is not adversely affected.

A clear background in the observation window is considered an internal negative control. However, when the stool samples are tested, the background may appear slightly yellowish due to the original color of the stool samples. This is acceptable as long as it does not interfere with the interpretation of test result. The test is invalid if the background fails to clear and obscures the reading of the result.

10. RESULTS

Test result is evaluated as “positive”, if two lines appears.

Positive: 2 pink-colored lines appear; one in the control region (C) and one in the test region (T) in either Hb and/or Hb/Hp tests.

If you are testing strongly positive samples, the intensity of the control line may be reduced. It is not recommended to compare the intensity of the lines.

Negative: 1 pink-colored line appears in the control region (C) in either Hb and/or Hb/Hp tests.

Invalid: If no red line appears in the control region in either Hb and/or Hb/Hp tests, this is a sign that the test is not functioning properly, or that the test materials are not correct. In this case, repeat the test with a new Test Cassette or contact the manufacturer for technical support.

11. LIMITATIONS OF THE PROCEDURE

A positive test occurs if human hemoglobin or hemoglobin/haptoglobin complex is present in the sample.

Not all intestinal bleeding are the result of benign or malignant polyps. The information that you obtain by performing this test should be examined in conjunction with other clinical findings and test methods.

Because carcinomas and polyps can bleed to different extents and intermittently in the case of immunological verification procedures, it is also advisable to test various stool samples from eg. three different days.

Urine and excessive dilution of samples with water from the toilet bowl can lead to false test results. It is therefore recommended that the Stool Collection paper be used.

Stool samples should not be taken during menstruation or 3 days before or after, in the case of bleeding caused by constipation, bleeding hemorrhoids, or in the case of medicine being administered rectally. This could lead to false positive results.

Blood-thinning medications such as, for example, acethylsalicylic acid or coumarin, as well as iron preparations, can lead to bleeding not caused by tumors. Such substances should be discontinued at least 48 hours prior testing.

12. PERFORMANCE CHARACTERISTICS

Analytical sensitivity

The limits of detection of the tests are 40 µg of the free hemoglobin and 40 µg of hemoglobin/haptoglobin complex per liter of buffer solution.

Prozone effect: The Hb and Hb/Hp complex test also works reliably at extremely high hemoglobin/haptoglobin values (>500 µg/L).

Specificity

The Biohit ColonView Hb and Hb/Hp test is specifically for human hemoglobin/haptoglobin and has no cross-reactivity with hemoglobin from cattle, pigs, rabbits, horses, or sheep at a concentration of up to 500 mg/L in the extraction buffer. The test also displays no cross-reactivity with Bilirubin, vitamin C, and horseradish peroxidase.

Note:

In a study of the Shinshu-University School of Medicine in Japan (11) the cost-value ratio of multiple measurements was examined (see below). It shows the relative sensitivity increases with the number of consequent tests, and its relative specificity decreases slightly.

Number of tests	sensitivity	specificity
1	58%	96%
2	89%	95%
3	100%	94%

13. REFERENCES

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10. van Rossum L et al. Random comparison of guaiac and immunochemical fecal occult blood screening for colorectal cancer in screening population. *Gastroenterology* 2008; 135: 82-90.
11. Yamamoto M.; Nakama H.; Cost-effectiveness analysis of immunochemical occult blood screening for colorectal cancer among three fecal sampling methods : *Hepatogastroenterology*; 2000 Mar-Apr; 47(32):396-9.

14. DATE OF ISSUE

ColonView Hb and Hb/Hp Test (30) insert.
Version 01, 22.10.2010.

15. WARRANTY

The Manufacturer shall remedy all defects discovered in any Product (the "Defective Product") that result from unsuitable materials or negligent workmanship and which prevent the mechanical functioning or intended use of the Products including, but not limited to, the functions specified in the Manufacturer's specifications for the Products. ANY WARRANTY WILL, HOWEVER, BE DEEMED AS VOID IF FAULT IS FOUND TO HAVE BEEN CAUSED BY MALTREATMENT, MISUSE, ACCIDENTAL DAMAGE, INCORRECT STORAGE OR USE OF THE PRODUCTS FOR OPERATIONS OUTSIDE THEIR SPECIFIED LIMITATIONS OR OUTSIDE THEIR SPECIFICATIONS, CONTRARY TO THE INSTRUCTIONS GIVEN IN THE INSTRUCTION MANUAL.

The period of this warranty for the Distributor is defined in the instruction manual of the Products and will commence from the date the relevant Product is shipped by the Manufacturer. In case of interpretation disputes the English text applies.

This Biohit diagnostic kit has been manufactured according to our ISO 9001 / ISO 13485 quality management protocols and has passed all relevant Quality Assurance procedures related to this product.

16. ORDERING INFORMATION

ColonView Hb and Hb/Hp Test (30).
Cat. No. 602 250.

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17. EXPLANATION OF THE SYMBOLS USED IN LABELS

	For <i>in vitro</i> diagnostic use
	Catalogue number
	Batch code
	Use by
	Consult instructions for use
 2...30°C	Temperature limitation. Store at 2...30°C
	Do not re-use

Note:

Note:

18. SHORT OUTLINE OF THE PROCEDURE

Collect a random specimen of stool according to the instructions in the ColonView Sample Collection Bag.

*

Take the test cassette from the foil packaging immediately before performing the test. Mark the cassette with the name of the patient or with another form of identification.

*

Carefully shake the Sample Collection Tube to ensure that the stool sample mixes properly with the extraction solution.

*

Unscrew the protective cap. Take a paper towel and break the seal of the Sample Collection Tube with rotary motion or use a pair of scissors to cut the seal. Hold the collection container upright and add 3 drops of the solution into the round sample windows (S) of the cassette.

*

Read the results after 5 minutes. Strongly positive results may be evaluated even sooner. Evaluate the result a maximum of 15 minutes after dropping the solution onto the round sample window.