labs. The results from the Reference Laboratory agreed over 99% with expected results. Overall, the accuracy of hema-screen™ SPECIFIC Immunochemical Fecal Occult Blood Test is 98%.

Comparison Studies:

Fifty specimens were also tested in-house with hema-screen™ SPECIFIC Immunochemical Fecal Occult Blood Test and two predicate device at multiple hemoglobin levels. This procedure was repeated 3 times with 3 lots of hema-screen™ SPECIFIC; as well as, both of the predicate devices. The correlation between hema-screen™ SPECIFIC Immunochemical Fecal Occult Blood Test and the two predicate devices was over 99%.

LIMITATIONS OF THE PROCEDURE

hema-screen™ SPECIFIC is a valuable aid in the early detection of gastrointestinal bleeding disorders, particularly those in the colon and rectum. However, a test result may be negative even when disease is present since bowel lesions, including some colorectal cancers and significant polyps, may not bleed at all or may bleed intermittently, or the blood may not be uniformly distributed in a fecal specimen and therefore missed during collection.

hema-screen™ SPECIFIC results may be positive for samples from patients without significant bowel pathology. Usually the reasons for this are obscure but, in some cases, this may be because certain medications may cause gastrointestinal irritation resulting in occult bleeding. As with any FIT, a positive hema-screen™ SPECIFIC test result should not be considered as a conclusive diagnosis for gastrointestinal bleeding or pathology. The evidence base for the value of FIT concerns applications in preliminary screening, particularly of asymptomatic populations, or as an aid to diagnosis. They are not intended to totally replace other diagnostic procedures such as colonoscopy, flexible sigmoidoscopy, or other imaging investigations such as double contrast barium enema or CT colography.

REFERENCES

1. Winawer S, et al, for the U.S. Multisociety Task Force on Colorectal Cancer. Colorectal cancer screening and surveillance: Clinical guidelines and rationale - Update based on new evidence. Gastroenterology 2003;124:544-60.
2. Starkey BJ. Screening for colorectal cancer. Ann Clin Biochem 2002;39:351-365.
3. Allison WS, Tekawa IS , Ransom LJ, et al. A comparison of fecal occult-blood tests for colorectal cancer screening. N Eng J Med 1996;554:155-9.
4. Young GP, St. John JB, Winawer, SJ, Rozen P. Choice of fecal occult blood tests for colorectal cancer screening: recommendations based on performance characteristics in population studies. A WHO and OMED Report. Am J Gastroenterol 2002;97:2499-507.
5. Castiglione G, Zappa M, Grazzinin G, et al. Screening for colorectal cancer by faecal occult blood test: comparison of immunochemical tests. J Med Screen 2000;7:35-7.
6. Nakama H, Zhang B, Fattah ASMA. A cost-effective analysis of the optimum number of stool specimens collected for immunochemical occult blood screening for colorectal cancer. Eur J Cancer 2001;36:647-50.
7. Boad I. Uber Okkulte Mageriblutungen. Dtsch Med Wochenschr 1901; 27:315-321.
8. Van Deen J. Tincture guaijaci, and ein Ozontrager, als Reagens aufsehr eringe Blutmengen, namentlich in medicoforensischen fallen. Arch Holland BeitrKatura F ilk 984; 3:228-231.
9. Adams EC, Layman KM. Immunochemical confirmation of gastrointestinal bleeding. Ann EHN Lab Sci 1974; 4:343.
10. Salto H, et al. An immunological occult blood test for mass screening of colorectal cancer by reverse-passive hemagglutination (RPI-IA). Jap J Gastroenterology 1984; 61:2831.
11. Heinrich HC. Ultrasensitiver immunochemistry okkultblutnach weis im Stuhl. In: Fruhmorgen P (ed) Prevention and Fruherkennung des kolorektalen Karinoms, 1st end. Springer, Berlin Heidelberg New York, 1984; pp. 59-82.

CE Mark/CE-Zeichen/ Marca CE/Marque CE

Immunostics, Inc.

1750 Brielle Ave., A5
Ocean, NJ 07712

3505 Sunset Ave.
Ocean, NJ 07712

Phone: (732) 918-0770
Fax: (732) 918-0618

EC REP

MediMark® Europe SARL
European Headquarters Operation
11, rue Emile Zola-BP 2332
38033 Grenoble Cedex 2-France
Phone: 33 (0)4 76 86 43 22
Fax: 33 (0)4 76 17 19 82
Email: info@medimark-europe.com

immunostics, inc.

PS-378 rev 09 03/2015

hema-screen™ SPECIFIC

Immunochemical Fecal Occult Blood Test
With DEVEL-A-TAB Sampler

CLIA COMPLEXITY: WAIVED

INTENDED USE

hema-screen™ SPECIFIC, a Fecal Immunochemical Test (FIT) is a rapid, convenient qualitative immunoassay for the determination of human hemoglobin in feces, a vital tool in the diagnosis and therapy of gastrointestinal disorders. hema-screen™ SPECIFIC features an innovative sampling method that utilizes one card for collection of two (2) specimens of feces and ONLY one immunochemical specimen preparation tube/test cassette system for analysis.

SUMMARY AND EXPLANATION

Colorectal cancer guidelines published in the US and elsewhere stress the importance of regular screening of people age 50 and older. A number of screening approaches are possible. Traditionally, guaiac FOBT methods have been used and there are data that show a reduction in the risk of death from colorectal cancer through repeated screening with this type of test. However, guaiac tests have low clinical sensitivity and low specificity. People who have cancer and polyps can have negative guaiac FOBT test results. Moreover, false positive results due to dietary substances including meat and certain fruits, drugs, and other causes are common, and these may lead to unnecessary invasive investigation. For this reason, recent regional and national screening programs, newer publications, and current guidelines have strongly supported the use of immunochemical FIT tests directed towards detection of the globin component of human hemoglobin in feces. There is ever growing evidence that immunochemical FOBT tests using one or two samples of feces have improved sensitivity (a lower number of false positives) while maintaining acceptable specificity (a higher number of true positives). Moreover, no dietary restriction is required, unlike the newer more sensitive guaiac FOBT tests. In addition, because the test detects globin rather than being based on the peroxidase activity of hemoglobin, FIT detects colorectal malignancies rather than gastric malignancies or upper GI problems. The use of two samples of feces has been shown to be optimum. The DEVEL-A-TAB Sampler facilitates collection of two samples of feces that are assayed together using a single specimen preparation tube/test cassette system providing a time efficient and cost effective screening method. In addition, hema-screen™ SPECIFIC detects lower concentrations of fecal occult blood than the standard guaiac FOBT by employing an immunospecific, double-sandwich capture method.

PRINCIPLE

hema-screen™ SPECIFIC is a qualitative, sandwich dye conjugate immunoassay that employs a unique combination of monoclonal and polyclonal antibodies to selectivity identify the globin component of human hemoglobin in fecal specimens with a high degree of analytical sensitivity. Two samples of feces, collected using the unique DEVEL-A-TAB Sampler, are dispersed in a single tube containing a known volume of buffer. The unique design of the Sampler ensures that a controlled amount of feces is added to the specimen preparation tube. Then, the feces in buffer is transferred to the test cassette detection system using the tube itself as the delivery system. In less than five minutes, unusually elevated concentrations of human hemoglobin in feces can be detected and positive results for abnormal concentrations of hemoglobin can be seen in the test cassette detection system as early as two or three minutes after application of specimen. As the feces in buffer specimen flows up through the absorbent device, the labeled antibody-dye conjugate binds to the globin of hemoglobin in the specimen forming an antibody-antigen complex. This complex binds to anti-globin antibody in the positive test reaction zone and produces a pink-rose color band. In the absence of hemoglobin, there is no line in the test reaction zone. The pink-rose color bands in the control reaction zone demonstrate that the reagents and devices are functioning correctly. In the extremely rare event of operator or test cassette failure, sufficient specimen is available in the tube to repeat the procedure with another test cassette.

REAGENTS

1. hema-screen™ SPECIFIC, one test cassette per foil pouch, that contains a combination of mouse monoclonal antibodies and polyclonal antibodies (sheep or goat) directed against the globin of human hemoglobin. Mouse monoclonal antibody on a colloidal gold particle.
2. Buffer solution in specimen preparation tube. (PBS with 0.1% Sodium Azide)
   Warning: Do not swallow – if spilled, wash with copious amounts of water.

MATERIALS PROVIDED

- hema-screen™ SPECIFIC test cassette in foil pouch with desiccant.
- Buffer solution in specimen preparation tube. (PBS with 0.1% Sodium Azide)

- Patient mailing envelope containing:
  1. DEVEL-A-TAB Sampler,
  2. patient instructions,
  3. collection tissues, and
  4. applicator sticks.

MATERIAL NEEDED BUT NOT PROVIDED

Timer, disposable gloves, and (optional) vortex or rotator. No other equipment or reagents are needed.

STORAGE

Specimen preparation tubes should be stored at up to 30°C (room temperature) until use. Store test cassette at up to 30°C (room temperature). The test cassette is stable until the expiration date imprinted on the pouch label.

NOTES AND PRECAUTIONS

1. The test is intended for IN VITRO DIAGNOSTIC USE ONLY.
2. Read directions for use carefully before performing this test procedure.
3. Do not use the test beyond the expiration date indicated on the pouch label.

QUALITY CONTROLS

INTERNAL QUALITY CONTROL

Internal procedural controls are included in the test. A red line appearing in the contol region (C) is an internal positive procedural control. It confirms sufficient volume and correct procedural technique. A clear background is an internal negative procedural control. If the test is working properly, the background in the result area should be white to light pink and not interfere with the ability to read the test result.

EXTERNAL QUALITY CONTROL

Good laboratory practice recommends running positive and negative external controls per lot per shipment or as often as the needs of the laboratories dictate.

SPECIMEN COLLECTION PROCEDURE (s)

There are two approved methods of fecal specimen collection:

METHOD #1

Advantages of the first method utilizing the DEVEL-A-TAB sampler are as follows: thirty (30) days stability; and if the card is not returned the buffer tube and cassette are still useable. In addition, the replacement of the DEVEL-A-TAB sampler and mailing costs are reduced in comparison to the replacement of the buffer tube.

Patient using DEVEL-A-TAB Sampler collects specimens at home over the course of two consecutive bowel movements exactly as per the Patient's Directions for Use detailed on the Sampler. The DEVEL-A-TAB Sampler is returned to the physician or laboratory, as directed, in the US Postal approved sealable mailing envelope provided.

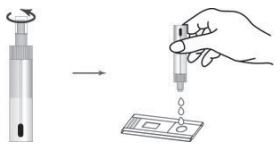
TEST PROCEDURE

1. Take DEVEL-A-TAB Sampler, remove DEVEL-A-TAB sample strip slowly and drop into uncapped specimen preparation tube; replace cap.

2. Tighten the cap thoroughly and lay tube flat allowing buffer to cover sample strip for at least 3 minutes. Use stick attached to tube cap to loosen feces from sample strip if dispersion of specimen seems inadequate. Shake the tube vigorously (or vortex or rotator mix) to ensure the feces is well mixed with the buffer. Some small amount of fecal matter may not go into solution.

NOTE: The DEVEL-A-TAB Sampler specimen is stable at room temperature for 30 days from the earliest collection date. It is recommended that once the specimen is dispersed in the preparation buffer tube that the test is analyzed by the day's end.

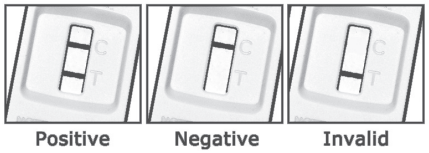
3. Remove test cassette device from its foil wrapper by tearing along the notch.
4. Tap the specimen preparation tube on a hard surface to dislodge any trapped air in top of cap.
5. Invert tube a number of times to ensure all undissolved fecal matter is dispersed in the buffer. Unscrew tip cap on the specimen preparation tube. Squeezing the tube slightly, dispense three (3) drops into test cassette well.



6. If the buffer flow along the test cassette appears to have stopped, tap cassette lightly on a hard surface, if flow does not continue, dispense one or more further drops into the test cassette well.
7. Read results at five minutes after the addition of specimen to the test cassette well.

INTERPRETATION OF RESULTS

1. Positive: one color line appearing in the "C" area, another color line in the "T" area.
2. Negative: Only one color line appearing in the "C" area, NO color line in the "T" area.
3. Invalid: If no color line appears in "C" area, the test result is invalid and further analysis of the specimen remaining in the preparation tube should be done with a new test cassette.

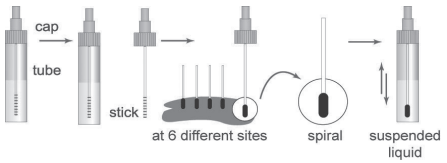


METHOD #2

The alternate specimen collection offers a familiar and well known procedure utilizing the buffer tube and cassette without the DEVEL-A-TAB sampler.

1. Loosen cap of specimen preparation tube and remove cap with its integral stick.
2. Introduce the stick into the fecal sample six times at different sites. In order to get sampling even in the spirals of the stick and to ensure appropriate specimen to buffer ratio, try to avoid obtaining clumps of fecal matter.
3. Return the stick to the specimen preparation tube. Tighten the cap thoroughly and shake the tube so as to disperse the specimen throughout the buffer in the tube.

NOTE: Handle and dispose of all specimens for testing as if potentially infectious. Proper precautions in handling and disposal should be maintained according to good laboratory practice and local or national regulations or requirements should be followed. If not to be used immediately after addition of fecal sample, specimen preparation tube should be refrigerated but must be analyzed using the test cassette within 14 days.



PROCEDURE

Follow steps 3 through 7 in TEST PROCEDURE above.

INTERPRETATION OF RESULTS

1. Positive: One color line appearing in the "C" area, another color line in the "T" area.
2. Negative: Only one color line appearing in the "C" area, NO color line in the "T" area.
3. Invalid: If no color line appears in "C" area, the test result is invalid and further analysis of the specimen remaining in the preparation tube should be done with a new test cassette.

PERFORMANCE CHARACTERISTICS

ANALYTICAL DETECTION LIMIT

When using dilutions of material with known hemoglobin content assayed by standard reference methodology, the analytical detection limit (commonly known as sensitivity) of hema-screen™ SPECIFIC has been set at a concentration of 50 ng Hb/mL buffer in order to achieve a high detection rate for disease. This is equivalent to 50 µg Hb/g feces, the analytical detection limit generally achieved with immunochemical FIT.

hema-screen™ SPECIFIC is specific for human hemoglobin; samples containing the following substances (expressed per mL of buffer) had no effect on the test result and were not detected.

Chicken hemoglobin	500 µg/mL
Pork hemoglobin	500 µg/mL
Beef hemoglobin	500 µg/mL
Goat hemoglobin	500 µg/mL
Horse hemoglobin	500 µg/mL
Rabbit hemoglobin	500 µg/mL
Radish Peroxides	2000 µg/mL

Accuracy:

Three Physicians Office Laboratories were supplied with sufficient kits to perform a minimum of 100 determinations. Of the 100 samples, 50 were supplied as Devel-A-Tab® format and 50 in the standard tube format. Sixty percent of the samples were spiked with levels of hemoglobin (0, 37.5, 50, 62.5 & 2000 µg hHb/g feces). The blinded specimens were tested with hema-screen™ SPECIFIC Immunochemical Fecal Occult Blood Test at Physicians Office Laboratories and a Reference Laboratory.

Accuracy of this device in the POL study, by qualified personnel with diverse educational background and work experience, was over 99% agreement with both sampling methods; 100% inter-day reproducibility; as well as, over 99% agreement between the