510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE AND INSTRUMENT TEMPLATE

A. 510(k) Number:
k041408

B. Purpose for Submission:
Marketing this test in the US

C. Analyte:
Human Hemoglobin

D. Type of Test:
Analyzer to perform an automated immunological test for the qualitative detection of antibodies for human hemoglobin

E. Applicant:
Polymedco, Inc.

F. Proprietary and Established Names:
OC Auto Micro FOB Test and Polymedco OC Auto Micro 80 Analyzer

G. Regulatory Information:

1. Regulation section:
   21 CFR § 864.6550
2. Classification:
   Class II
3. Product Code:
   KHE-Reagent, Occult Blood
4. Panel:
   Hematology 81

H. Intended Use:

1. Intended use(s):
   The Polymedco OC Auto Micro 80 Analyzer and OC Auto Micro FOB Test are designed to be used together as an immunological test system intended for the qualitative detection of fecal occult blood in feces by professional laboratories. The automated test is useful for the determination of gastrointestinal (GI) bleeding, found in a number of gastrointestinal (GI) disorders, e.g., colitis, polyps, and colorectal cancer.

2. Indication(s) for use:
   The OC Auto Micro FOB Test is recommended for use in 1) routine physical examinations, 2) monitoring for bleeding in patients, and 3) screening for colorectal cancer or gastrointestinal bleeding.

3. Special condition for use statement(s):
   N/A

4. Special instrument Requirements:
   Polymedco OC Auto Micro 80 Analyzer

I. Device Description:

The OC Auto Micro FOB Test kit consists of sampling bottles containing an extraction buffer. The sample bottles are then placed on the OC Auto Micro 80 Analyzer where an automated immunoassay is performed using the test kit reagents.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Alfa Scientific Instant-View Fecal Occult Blood Rapid Test
2. Predicate K number(s):
   K021423
3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Test Principle	Immunoassay utilizing antibodies for the detection of human hemoglobin	Immunoassay utilizing monoclonal antibodies for the detection of human hemoglobin
Sample	Feces in an extraction buffer	Feces in an extraction buffer
Intended Use	Qualitative detection of fecal occult blood in feces by professional laboratories	Qualitative detection of fecal occult blood in feces by laboratories or physician's offices
Differences		
Item	**Device**	**Predicate**
Test Device	Automated immunoassay using latex fixation	Manual immunoassay lateral flow test strip system
Extraction Buffer	HEPES buffer	PBS Buffer
Test Cut-off	100 ng/mL	50 ng/mL
Detection	Optical measurement of agglutination of latex particles	Presence of visible line formed by chromatographic assay

Calibration	Calibrator containing hHb A0 is serially diluted prior to analysis to construct a calibration curve	No calibration necessary

K. Standard/Guidance Document Referenced (if applicable):

"Review Criteria for the Qualitative Assessment of Fecal Occult Blood in Vitro Diagnostic Devices"

L. Test Principle:

The Polymedco OC Auto Micro FOB Test is an immunoassay utilizing monoclonal and polyclonal antibodies to specifically detect the presence of human hemoglobin in feces. The assay is designed to perform on the OC Auto Micro 80 Analyzer. Collected feces is scraped with the sampling probe and placed into the sample bottle containing the extraction buffer. The sample bottle containing the resulting fecal extract is then placed on the analyzer or the contents of the sample bottles are poured into sampling cups and placed on the analyzer.

The test reagent contains anti-human hemoglobin antibody attached to a polystyrene latex particle. When this reagent is added to the fecal extraction and agitated an antigen-antibody reaction begins and the particles agglutinate. The agglutination is measured as an optical change by the analyzer. The absorbance of the reaction mixture increases in proportion to the concentration of hemoglobin in the specimen. A calibration curve is created by dilution of a primary calibrator that contains a known concentration of hemoglobin. The curve is created by plotting the known concentration against the absorbance values. The concentration of hemoglobin is then determined by reading the unknown absorbance values off of the standard curve. The results are presented as Positive or Negative.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Reproducibility

Stool extract samples were spiked with human hemoglobin at five different concentrations: 0, 30, 50, 100, and 2000 ng/mL. Eight replicates of each concentration were prepared to total forty stool extraction samples. Samples were tested with three lots of the OC Auto Micro FOB Test. Results are acceptable and are presented below.

EIKEN OC Auto Micro FOB Test Lot: 36003 Results					
	SPIKED Hb CONCENTRATION IN STOOL EXTRACT				
Replicate	O ng/mL	3O ng/mL	5O ng/mL	10O ng/mL	200O ng/mL
1	NEG	NEG	NEG	POS	POS
2	NEG	NEG	NEG	POS	POS
3	NEG	NEG	NEG	POS	POS
4	NEG	NEG	NEG	POS	POS
5	NEG	NEG	NEG	POS	POS

6	NEG	NEG	NEG	POS	POS
7	NEG	NEG	NEG	POS	POS
8	NEG	NEG	NEG	POS	POS

EIKEN OC Auto Micro FOB Test Lot:: 3X004 Results					
	SPIKED Hb CONCENTRATION IN STOOL EXTRACT				
Replicate	O ng/mL	3O ng/mL	5O ng/mL	10O ng/mL	200O ng/mL
1	NEG	NEG	NEG	POS	POS
2	NEG	NEG	NEG	POS	POS
3	NEG	NEG	NEG	POS	POS
4	NEG	NEG	NEG	POS	POS
5	NEG	NEG	NEG	POS	POS
6	NEG	NEG	NEG	POS	POS
7	NEG	NEG	NEG	POS	POS
8	NEG	NEG	NEG	POS	POS

EIKEN OC Auto Micro FOB Test Lot:: 41001 Results					
	SPIKED Hb CONCENTRATION IN STOOL EXTRACT				
Replicate	O ng/mL	3O ng/mL	5O ng/mL	10O ng/mL	200O ng/mL
1	NEG	NEG	NEG	POS	POS
2	NEG	NEG	NEG	POS	POS
3	NEG	NEG	NEG	POS	POS
4	NEG	NEG	NEG	POS	POS
5	NEG	NEG	NEG	POS	POS
6	NEG	NEG	NEG	POS	POS
7	NEG	NEG	NEG	POS	POS
8	NEG	NEG	NEG	POS	POS

Intra Assay Precision

Three levels of sample were tested; low control, mid-level control, and high control. Ten replicates of each of the three samples were tested over two analytical runs. The mean, standard deviation (SD) and coefficient of variation (CV) were calculated. The intra assay acceptance criteria was a CV of <5%. The results are acceptable with the CV's for each level of control less than 5%.

Inter Assay Precision

The instrument was calibrated only once prior to the testing of the materials. Three levels of sample were tested; low control, mid-level control, and high control. Each sample was tested once per day over 20 days. The mean, standard deviation (SD) and coefficient of variation (CV) was calculated. The inter assay acceptance criteria was a CV of <10%. The results are acceptable with the CV's for each level of control less than 5%.

Instrument to Instrument Precision

Two OC Auto Micro 80 Analyzers were utilized using one level of sample, low control, in three runs of ten replicates each over three days. Upon completion of the testing the data for each day was combined, totaling 90 data

points per sample per instrument. The mean, standard deviation (SD) and coefficient of variation (CV) were calculated. The data sets were also analyzed for overlapping 95% confidence limits and normal distribution patterns in a P-Plot and histograms. Statistical analysis of the data from the instrument-to-instrument study suggests that there is no statistical difference between the results generated by the two instruments. The low control sample produced acceptable results (P value=0.546) and each instrument produced acceptable individual results with all CV's <5%.

b. Linearity/assay reportable range:
N/A

c. Traceability (controls, calibrators, or method):
The calibrator contains 1 mL of human hemoglobin (A0) extract at a concentration of 1920 ng/mL. The calibrator is serially diluted prior to analysis with a Standard Diluent buffer to construct a calibration curve.

The negative control contains 5 mL of buffer. The positive control contains 5 mL of 200 ng/mL purified hemoglobin in buffer.

The control and calibrator materials were tested and found negative for Human immunodeficiency virus (HIV) 1 and 2, Hepatitis B virus (HBV) and Hepatitis C virus (HCV). The tests used were cleared for *in-vitro* diagnostic use by the Ministry of Health in Japan.

d. Detection limit:
N/A

e. Analytical specificity:
<u>Animal hemoglobins and tissues</u>
A performance study ws completed to investigate the cross reactivity of other species of hemoglobin (Hb) and issue extracts on the OC Auto Micro FOB Test and Alfa Instant View device (predicate). Hemoglobins of bovine, equine, pig, rabbit, sheep, fish, chicken and goat origin were added to the test device to determine the cross reactivity of the test with hHb of other species. Each Hb species was added to normal stool extracts with both 0 and 100 ng/mL hHb concentrations. No cross reactivity was evident. The negative results continued to be negative and the positive results continued to be positive after the addition of the animal hemoglobins. The study was repeated with tissue extracts of beef, pig, rabbit, sheep, fish, chicken and goat and no cross reactivity was evident.

<u>Human hemoglobin</u>
A study was completed to investigate the performance of the OC Auto Micro FOB Test and Alfa Instant View device (predicate) with

abnormal blood samples. Two types of abnormal blood were tested (Thalassemia and Sickle Cell) and the results compared to Normal human hemoglobin (hHb). Stool extract samples were spiked with whole human blood (approximately 14.6 g/dL of hemoglobin) at four different concentrations: 0, 25, 50, and 150 ng/mL. At the concentrations of 0, 25, and 50 ng/mL the OC Auto Micro FOB Test was consistently negative and at the concentration of 150 ng/mL the OC Auto Micro FOB test was consistently positive. The studies suggest that there are no false negative issues measuring hemoglobin variants found in Thalassemia or Sickle Cell diseases.

Dietary substances

A performance study was completed to investigate the interference of dietary substances on the OC Auto Micro FOB Test and Alfa Instant View device (predicate). Aqueous extracts of raw broccoli, cauliflower, cantaloupe, horseradish, red radish, parsnip, and turnip were added to the test device to determine if vegetable extracts cross react with the test. The extracts were prepared by homogenizing raw vegetables in a food processor and then subsequently centrifuging the extract to separate the solid and liquid phases. Dietary Iron and Vitamin C supplements and horseradish peroxidase were also tested for cross reactivity. The dietary substance extracts were added to normal stool extracts at both 0 and 100 ng/mL hHb. The OC Auto Micro FOB Test and predicate device produced acceptable results for the interference of dietary substances study. All of the 0 ng/mL hHB samples spiked with an interfering substance produced negative results. All of the 100 ng/mL hHb samples spiked with an interfering substance were positive on the OC Auto Micro FOB Test and predicate devices.

Toilet water

Toilet water was tested with the presence of various clearners, from enzymatic to sodium hypochlorite based. Toilet water was added to normal stool extracts at both 0 and 100 ng/mL human hemoglobin. All of the 100 ng/mL hHb samples spiked with toilet water samples were positive on the OC Auto Micro FOB test and all the 0 ng/mL HB samples spiked with toilet water continued to be negative on the OC Auto Micro FOB test.

Contaminants

A residual concentration equal to 100 ng/mL of Hb that remains in the toilet water will produce a false positive result when introduced to the OC Auto Micro FOB Test. It is suggested to avoid contact with the toilet water during the collection process. The specimen should be collected on clean paper or in a clean container for sampling.

f. Assay cut-off:
The cut-off for the OC Auto Micro FOB Test was determined by assaying thirty replicates of each of sixteen known concentrations of purified human hemoglobin diluted in a buffered diluent. The buffered diluent was also tested along with the control solutions. The specificity and sensitivity was calculated at each concentration. The cut-off was chosen where the sensitivity and specificity were maximized. The cut-off was determined to be 100 ng/mL. At 100ng/mL there was a sensitivity of 96.11% (346/360) and a specificity of 99.33% (149/150).

2. Comparison studies:

a. Method comparison with predicate device:
Stool extract samples were spiked with human hemoglobin at five different concentrations: 0, 30, 50, 62.5, and 2000 ng/mL, eight replicates were prepared and tested with the OC Auto Micro FOB test and the Alfa Scientific test (predicate device). There was 100% agreement between the results obtained from the predicate and test device.

b. Matrix comparison:

3. Clinical studies:

a. Clinical sensitivity:

b. Clinical specificity:

c. Other clinical supportive data (when a and b are not applicable):
Comparison with predicate device
63 samples from patients with positive diagnoses were tested with the predicate and the test device. There was 100% agreement between the test and predicate device for the positive samples.

106 asymptomatic patients were tested with the test and the predicate device. All test device results were negative. There was 99% (105/106) agreement between the test and predicate devices.

4. Clinical cut-off:
N/A

5. Expected values/Reference range:
N/A

N. Instrument Name:
Polymedco OC Auto Micro 80 Analyzer

O. System Descriptions:

1. Modes of Operation:
   Closed tube
2. Software:

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:
Yes ____X____ or No _____

3. Sample Identification:
   Manual (loading list) or Barcode reader
4. Specimen Sampling and Handling:
   Pierced cap
5. Assay Types:
   Immunoassay
6. Reaction Types:
   latex agglutination reaction.
7. Calibration:
   Hemoglobin derived from human blood is serially diluted to create a calibration curve.
8. Quality Control:
   Positive and negative controls are provided. It is the responsibility of the operator to run controls and ensure that the assay is functioning properly.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "L. Performance Characteristics" Section Of The SE Determination Decision Summary:

Q. Conclusion:
The submitted material in this premarket notification is complete and support a substantial equivalence decision.