510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K170548

B. Purpose for Submission:

To modify the fecal sample collection procedure

C. Measurand:

Human hemoglobin (hHb) in feces

D. Type of Test:

Lateral flow chromatographic immunoassay

E. Applicant:

Enterix Inc., A Clinical Genomics Inc. Company

F. Proprietary and Established Names:

InSure ONE – One Day Fecal Immunochemical Test

G. Regulatory Information:

1. Regulation section:

   21 CFR 864.6550, Occult blood test

2. Classification:

   Class II

3. Product code:

   KHE, Reagent, Occult Blood

4. Panel:

   Hematology (81)

H. Intended Use:

1. Intended use:

   The InSure ONE is a fecal immunochemical test (FIT) that qualitatively detects human hemoglobin from blood in fecal samples. The samples will generally be collected by the test subject at home and the test developed at laboratories or professional offices. The InSure ONE test is used to aid in the detection of lower gastrointestinal bleeding.

2. Indication(s) for use:

   Same as Intended Use

3. Special conditions for use statement(s):

   For prescription use and over-the-counter (sample collection kit)

4. Special instrument requirements:

   Not applicable

I. Device Description:

The InSure ONE – One Day Fecal Immunochemical Test qualitatively detects human hemoglobin from blood in fecal samples. The fecal sample is generally collected by the test subject at home. Stool samples in toilet bowl water are collected using long handled brushes to collect a small volume of water from around the defecated stool. Once collected, the stool sample is placed on an InSure ONE Test Card. The InSure ONE Test Card then serves as a means to transport the dried stool sample to the laboratory. The test reaction is developed in the clinical laboratory or medical professional office with appropriate quality control.

Components of InSure ONE – One Day Fecal Immunochemical Test:

a. The InSure ONE Collection Kit contains:

   - InSure ONE Instructions for Use-Patient
   - InSure ONE Test Card
   - Brush Kit containing 2 brushes and a waste bag
   - Business reply form and envelope

b. The InSure ONE Developer Components (for development and interpretation of the test) contains:

   - InSure ONE Instructions for Use-Professional Laboratory

- InSure Test Strips: The Test Strips contain a mouse monoclonal anti-human hemoglobin Test Line and a conjugate-specific polyclonal (donkey anti-goat) antibody Control Line and a conjugate of anti-human hemoglobin polyclonal antibodies bound to colored (colloidal gold) particles.
- InSure Run Buffer: Contains borate salts, ethanol, bovine serum albumin, and sodium azide as preservative.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   InSure FIT Fecal Immunochemical Test

2. Predicate 510(k) number(s):

   K002457

3. Comparison with predicate:

Similarities		
Item	Device InSure ONE – One Day Fecal Immunochemical Test, K170548	Predicate InSure FIT Fecal Immunochemical Test, K002457
Intended Use	The InSure ONE is a fecal immunochemical test (FIT) that qualitatively detects human hemoglobin from blood in fecal samples. The samples will generally be collected by the test subject at home and the test developed at laboratories or professional offices. The InSure ONE test is used to aid in the detection of lower gastrointestinal bleeding.	InSure™ FOBT is an immunochromatographic fecal occult blood test that detects human hemoglobin from blood in fecal samples. The samples will generally be collected by the test subject at home and the test developed at laboratories or professional offices. The InSure™ FOBT sample collection kit, consisting of a) Test Kit Envelope, b) Instructions for Use; c) Test Card, d) Brush Kit, e) Reply Form, f) Return Envelope, and g) Screening for Life brochure, is intended for Over-The-Counter distribution. Fecal occult blood test are useful screening aids for detecting primarily lower gastrointestinal (g.i.) disorders that may be related to iron deficiency anemia, diverticulitis, ulcerative colitis, polyps, adenomas, colorectal cancers or other g.i. lesions that can bleed. InSure™ FOBT is recommended for use by health professionals as part of routine physical examinations and in

Similarities		
Item	Device InSure ONE – One Day Fecal Immunochemical Test, K170548	Predicate InSure FIT Fecal Immunochemical Test, K002457
		screening for colorectal cancer or other sources of lower g.i. bleeding.
Sample Type	Feces	Same
Test Principle	Qualitative test system intended for immunochemical detection of fecal occult blood in feces.	Same
Detection Method	Lateral flow chromatographic immunoassay	Same
Assay Cut-off	50 μg hemoglobin/g stool	Same

Differences		
Item	Device InSure ONE – One Day Fecal Immunochemical Test, K170548	Predicate InSure Fecal Immunochemical Test, K002457
Sample Collection	Patient collects and transfers two samples of toilet bowl water from one bowel movement to the test card.	Patient collects and transfers two samples of toilet bowl water from two different bowel movements to the test card.

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

CLSI EP12-A2 User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline- Second Edition, 2008.

L. Test Principle:

The InSure ONE Test uses the principle of immunochromatography to detect human hemoglobin in samples of toilet bowl water collected from around the stool after defecation. The test result is obtained from *one* stool sample. The toilet bowl water is collected after brushing the surface of the stool to release any blood into the surrounding water. Long handled brushes are used to collect and transfer two samples of toilet bowl water from *one* bowel movement to the InSure ONE Test Card. The InSure ONE Test Card is used to transport the dried sample to the testing site. At the testing site, an immunochromatographic Test Strip is inserted into the Test Card and Run Buffer is added to rehydrate the sample and to extract the hemoglobin, if present, from the sample. The sample flows along the InSure ONE Test Strip, rehydrates the colloidal gold anti-human hemoglobin conjugate and, if hemoglobin is present, forms a hemoglobin-conjugate immune complex. The complex is then captured on the Test Strip, in a zone containing immobilized anti-human hemoglobin antibodies, to form a visible test line – a positive test. No test line is indicative of the absence of human hemoglobin in the sample – a negative test. Unbound conjugate continues to migrate along the InSure ONE Test Strip and binds to the control line, which contains conjugate-specific antibodies. The control line confirms that the reagent flow is complete and the test is functional.

M. Performance Characteristics:

1. Analytical performance:

a. Precision/Reproducibility:

Please refer to K002457.

b. Linearity/assay reportable range:

Please refer to K002457.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Internal Control
Procedural controls are included in the test device. It confirms sufficient specimen volume and correct procedural technique.

External Controls
It is recommended that positive and negative controls be performed to verify proper test performance. External controls are not provided with the test kit.

d. Detection limit:

Not applicable

e. Analytical specificity:

Please refer to K002457.

f. Assay cut-off:

Fecal test samples were prepared by spiking stool samples with human blood of known hemoglobin concentration, to obtain the following fecal hemoglobin concentrations: 0 µg Hb/g stool, 5 µg Hb/g stool, 10 µg Hb/g stool, 20 µg Hb/g stool, 30 µg Hb/g stool, 40 µg Hb/g stool, 50 µg Hb/g stool, 60 µg Hb/g stool and 80 µg Hb/g stool. Pre-measured quantities of stool spiked with different levels of hemoglobin were placed in a pre-measured volume of water to simulate toilet water in which stool will be deposited. Following deposition of the stool, water samples were taken at 2 minutes with the InSure sample collection brushes and applied to Test Cards using the InSure FIT and the InSure ONE sampling procedures. Testing was performed side-by-side with the predicate by comparing the test results of the device with that of the predicate. Test Cards were prepared on Day 0, stored at room temperature (20–25°C) and developed on Day 5 to simulate the time span between the patient collecting the fecal water sample on the Test Card and transporting the sampled Test Card to the laboratory by mail. The cut-off was determined to be 50 µg hemoglobin/g stool.

Table 1. Assay Cut-off Study

Hb Concentration (µg Hb/g stool)	N	InSure ONE		Negative Percent Agreement (95% CI)	Positive Percent Agreement (95% CI)
		Negative	Positive		
0	40	40	0	100% (91.2% – 100%)	0% (0% – 8.8%)
5	40	38	2	95.0% (83.5% – 98.6%)	5.0% (1.4% – 16.5%)
10	40	31	9	77.5% (62.5% – 87.7%)	22.5% (12.3% – 37.5%)
20	40	19	21	47.5% (32.9% – 62.5%)	52.5% (37.5% – 67.1%)
30	40	8	32	20.0% (10.5% – 34.8%)	80.0% (65.2% – 89.5%)
40	40	3	37	7.5% (2.6% – 19.9%)	92.5% (80.1% – 97.4%)
50	40	1	39	2.5% (0.4% – 12.9%)	97.5% (87.1% – 99.6%)
60	40	1	39	2.5% (0.4% – 12.9%)	97.5% (87.1% – 99.6%)
80	40	0	40	0% (0% – 8.8%)	100% (91.2% – 100%)

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison between the InSure ONE and the predicate test–InSure FIT, was conducted to determine if there was a significant difference in test performance between sampling two separate fecal samples once each or a single fecal sample, sampled twice, for detection of occult blood. Patients were recruited from three intended use sites and the study was performed at one intended use site in Australia. The study included an enriched population of patients with gastrointestinal symptoms or a history of past colorectal disease that were scheduled to have a colonoscopy for any reason:

- Patients in an endoscopy unit at a large public hospital that maintained a database of individuals under surveillance, based on their family history or personal history of colorectal cancer or adenomas.
- Patients from the general population based on referral to colonoscopy from their general practitioners for a prior positive fecal occult blood test or other indication.
- Patients from the general population with GI related conditions (i.e., abdominal pain,

anemia, constipation, diarrhea, diverticulitis, frank rectal bleeding or other GI symptoms).

A total of 859 patients (ages 20 – 93 years old) collected fecal water samples using the InSure FIT (Test Card A) and InSure ONE (Test Card B and Test Card C) prior to colonoscopy. Tissue samples collected at colonoscopy were histopathologically examined for the type of lesion (i.e., cancer, advanced adenoma, etc.). Statistical analysis of the test results for clinical positive percent agreement (PPA) and clinical negative percent agreement (NPA) showed that the InSure ONE test results have acceptable overall agreement with the InSure FIT test results. The study demonstrated that there were no statistically significant differences in the test results obtained from two fecal water sample aliquots taken from one bowel movement (new sampling method with InSure ONE), when compared to one fecal water sample aliquot taken from two separate bowel movements (predicate sampling method with InSure FIT).

Table 2. Patients with Colonoscopy

Colonoscopy	**N**	**%**
Colonoscopy Completed-Diagnosis Available	957	100
Colonoscopy and InSure FIT Results Available	895	93.5
Colonoscopy, InSure FIT Results & Histopathology Reports Available	859	89.8

Table 3. Patients with Colonoscopy and Histopathologic Diagnoses

Most Advanced Diagnosis (Colonoscopy & Histopathology)	**N**	**%**
Colorectal cancer	12	1.4
Advanced adenoma*	61	7.1
Non-advanced adenoma	111	12.9
Inflammatory bowel disease	27	3.1
Hemorrhoids	123	14.3
Diverticular disease	158	18.4
Hyperplastic polyp	38	4.4
Other GI finding	35	4.1
True Normal	294	34.2
Total	**859**	**100**

*≥10mm or high grade dysplasia or >2 adenomas or villous component or serrated phenotype.

Table 4. Summary of Agreement Between Test Card A and Test Card B

InSure FIT Test Card A		InSure ONE Test Card B			Overall Percent Agreement	Positive Percent Agreement (95% CI)	Negative Percent Agreement (95% CI)
Agreement	Test Card A	Positive	Negative	Total			
Overall	Positive	79	51	130	88.7% (86.4 – 90.6%)	63.2% (54.5 – 71.1%)	93.1% (91.0– 94.7%)
	Negative	46	683	729			
	Total	125	734	859			
Cancer	Positive	10	0	10	100.0% (75.8 – 100%)	100.0% (72.2 – 100%)	100.0% (34.2 – 100%)
	Negative	0	2	2			
	Total	10	2	12			
Advanced Adenoma	Positive	12	7	19	80.6% (69.6 – 88.3%)	63.2% (41.0 – 80.9%)	87.5% (75.3 – 94.1%)
	Negative	6	42	48			
	Total	18	49	67			
Non-Advanced Adenoma	Positive	10	8	18	83.8% (75.6 – 89.6%)	55.6% (33.7 –75.4%)	89.7% (81.5 – 94.5%)
	Negative	9	78	87			
	Total	19	86	105			
Negative, Non-neoplastic	Positive	31	22	53	89.2% (85.7 – 92.0%)	58.5% (45.1 – 70.7%)	94.2% (91.1 – 96.3%)
	Negative	19	309	328			
	Total	50	331	381			
Negative, no findings on colonoscopy	Positive	17	13	30	90.8% (87.0– 93.6%)	56.7% (39.2 – 72.6%)	94.7% (91.3 – 96.8%)
	Negative	14	250	264			
	Total	31	263	294			
1 or 2 Non-Advanced Adenoma < 5 mm	Positive	1	4	5	78.2% (65.6 – 87.1%)	20.0% (3.6 – 62.4%)	84.0% (71.5 – 91.7%)
	Negative	8	42	50			
	Total	9	46	55			
1 or 2 Non-Advanced Adenoma > 5 mm < 10mm	Positive	9	4	13	90.0% (78.6 – 95.7%)	69.2% (42.4– 87.3%)	97.3% (86.2 – 99.5%)
	Negative	1	36	37			
	Total	10	40	50			

Table 5. Summary of Agreement Between Test Card A and Test Card C

InSure FIT Test Card A		InSure ONE Test Card C			Overall Percent Agreement	Positive Percent Agreement (95% CI)	Negative Percent Agreement (95% CI)
Agreement	Test Card A	Positive	Negative	Total			
Overall	Positive	75	55	130	89.2% (86.9 – 91.1%)	62.0% (53.1 – 70.1%)	93.6% (91.6 – 95.2%)
	Negative	38	691	729			
	Total	121	738	859			
Cancer	Positive	10	0	10	100.0% (75.8 – 100%)	100.0% (72.2 – 100%)	100.0% (34.2 – 100%)
	Negative	0	2	2			
	Total	10	2	12			
Advanced Adenoma	Positive	12	7	19	80.6% (69.6 – 88.3%)	63.2% (41.0 – 80.9%)	87.5% (75.3 – 94.1%)
	Negative	6	42	48			
	Total	18	49	67			
Non-Advanced Adenoma	Positive	10	8	18	87.6% (80.0 – 92.6%)	55.6% (33.7 – 75.4%)	94.3% (87.2 – 97.5%)
	Negative	5	82	87			
	Total	15	90	105			
Negative, Non-neoplastic	Positive	30	23	53	89.5% (86.0 – 92.2%)	56.6% (43.3 – 69.0%)	94.8% (91.9 – 96.7%)
	Negative	17	311	328			
	Total	47	334	381			
Negative, no findings on colonoscopy	Positive	12	18	30	91.2% (87.4 – 93.9%)	40.0% (24.6 –57.7%)	97.0% (94.1 – 98.5%)
	Negative	8	256	264			
	Total	20	274	294			
1 or 2 Non-Advanced Adenoma < 5 mm	Positive	1	4	5	83.6% (81.7 – 91.1%)	20.0% (3.6 – 62.4%)	90.0% (78.6 – 95.7%)
	Negative	5	45	50			
	Total	6	49	55			
1 or 2 Non-Advanced Adenoma > 5 mm < 10mm	Positive	9	4	13	92.0% (81.2 – 96.8%)	69.2% (42.4 – 87.3%)	100% (90.6 – 100%)
	Negative	0	37	37			
	Total	9	41	50			

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Not applicable

N. Instrument Name:

Not applicable

O. System Descriptions:

1. Modes of Operation:

Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

Yes _____ or No ___x_____

Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

Yes _____ or No ___x_____

2. Software:

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

Yes _____ or No __x_____

3. Specimen Identification:

Enter patient identification information manually on the label of the Test Card.

4. Specimen Sampling and Handling:

Two separate applications of the fecal water sample, taken from the same bowel movement using a new sample collection brush for each sample. The first fecal water sample is applied to window "1" and the second fecal water sample from the same bowel movement is applied to window "2" on the same Test Card. The sample flap is then sealed with the peel off label. The patient provides their name, date of birth and date the sample was collected on the label included in the instructions for use. The test sample is placed in Test Card in the envelope provided and returned to the laboratory or medical professional office either by mail or personal delivery.

5. Calibration:

   Not applicable

6. Quality Control:

   Internal Controls: Procedural controls are included in the test device. A pink line appearing the control region is considered as the internal procedural control. The internal procedural control confirms the following: the conjugate was properly hydrated and has flowed through the test and control line areas, the control line antibodies were immunoreactive, and the conjugate is intact. The test is invalid if the control line does not appear.

   External Control: It is recommended that positive and negative controls be performed to verify proper test performance. The Enterix Insure FIT FOBT Controls (positive and negative) cleared in K101831, are recommended for use as external controls.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports substantial equivalence decision.