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**510(k) SUMMARY OF SAFETY AND EFFECTIVENESS**  
***FlexSure*<sup>®</sup> *OBT* Immunochemical Fecal Occult Blood Test**

This 510(k) summary of safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990.

Manufacturer: SmithKline Diagnostics, Inc.  
1050 Page Mill Rd.  
Palo Alto, CA 94303-0105  
Attention: Ronald J. Schoengold

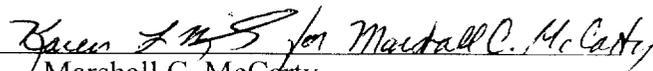
Proprietary Name: ***FlexSure*<sup>®</sup> *OBT***

Classification Name: Occult Blood Reagent

Intended Use: The ***FlexSure*<sup>®</sup> *OBT*** (Occult Blood Test) is a rapid, visually read, qualitative immunochemical chromatographic method for detection of human hemoglobin from blood in fecal samples. Fecal occult blood tests 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. ***FlexSure*<sup>®</sup> *OBT*** is recommended for use by health professionals as part of routine physical examinations or when lower g.i. disorders are suspected.

Predicate Product: **Hemocult**<sup>®</sup><sup>BRAND</sup> Routine Screening Test for Fecal Occult Blood Manufactured by SmithKline Diagnostics, Inc.

Performance Summary: The ***FlexSure*<sup>®</sup> *OBT*** Immunochemical Fecal Occult Blood Test is substantially equivalent to the predicate device Hemocult<sup>®</sup>, sold prior to May 28, 1976. The performance of ***FlexSure*<sup>®</sup> *OBT*** was verified by sensitivity, specificity, cross reactivity, interference, reproducibility and readability studies in laboratory and clinical settings. Refer to the attached PERFORMANCE CHARACTERISTICS.

  
Marshall C. McCarty  
Manager, Regulatory Affairs

10/28/96  
Date

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## *FlexSure*<sup>®</sup> *OBT* Immunochemical Fecal Occult Blood Test

### PERFORMANCE CHARACTERISTICS

#### Background

Fecal occult blood testing (FOBT) is utilized worldwide as a screening aid for persons 50 years of age or older to detect gastrointestinal (g.i.) bleeding disorders. Recent studies indicate that detection of 2 mL or more of daily g.i. blood loss can be an early indicator of significant lower g.i. pathology including colorectal neoplasia (adenomas  $\geq$  1 cm and colorectal cancers.)

#### Analytical Performance Studies

##### ANALYTICAL SENSITIVITY:

- ◆ **Lower Sensitivity Limit** - *In vitro* studies demonstrated that following the recommended procedures for sample collection and storage, *FlexSure*<sup>®</sup> *OBT* reliably detected 0.2 mL or more of added blood per 100 g of feces (0.3 mg hemoglobin per g of stool). This level of blood is approximately equal to 2 to 3 mL of daily *in vivo* lower g.i. bleeding.
- ◆ **Prozone Effect** - *In vitro* studies demonstrated that *FlexSure*<sup>®</sup> *OBT* reliably detected up to 17 mL of added blood per 100 g of feces (25 mg hemoglobin per g of stool). At this level and above, blood is generally visible in the stool.

##### ACCURACY OF TEST RESULTS:

- ◆ **Cross Reactivity Studies** - Individual fecal samples were spiked with horse myoglobin and hemoglobin from beef, chicken, fish, horse, pig, rabbit, goat, sheep and turkey to determine whether dietary substances cross react with the test. The *FlexSure*<sup>®</sup> *OBT* results were negative even at levels in excess of normal dietary intake or levels which consistently give false-positive results with guaiac-based tests.

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#### ACCURACY OF TEST RESULTS (continued):

- ◆ **Interference / Effect of Dietary Substances** - Fecal samples from different individuals spiked with excessive quantities of substances known to interfere with guaiac-based tests (plant peroxidases and ferrous iron to check for possible false-positive test results, and a mixture of vitamin C and human hemoglobin to check for possible false-negative test results) yielded 100% accurate test results with *FlexSure*<sup>®</sup> *OBT*.
- ◆ **Reproducibility** - The *within-site* and *between-site* reproducibility of *FlexSure*<sup>®</sup> *OBT* was demonstrated with a range of blood levels spiked into stool samples to give negative, borderline positive and positive test results. The *within-site* reproducibility was 100% (90/90). The *between-site* reproducibility was 97% (30/30 for the negative, 30/30 for the positive and 27/30 for the borderline positive sample).
- ◆ **Readability / Repeatability** - Comparable results were obtained with experienced and inexperienced reader groups, each using fecal samples spiked with low to moderate levels of human blood. The results indicated greater than 95% agreement among the two reader groups except at the analytical cutoff of the test where greater variation is expected. The "experienced" group was comprised of three SKD technicians who had used the test extensively, one with a doctorate degree and two with BA/BS degrees. The "inexperienced" group consisted of 16 individuals with varied educational backgrounds from High School to M.D. located in the U.S., Europe, Australia and Canada.

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### Clinical Performance Studies

#### AVERAGE RISK SCREENING:

- ◆ **Apparent Specificity and Positive Predictive Value in a Comparison of Paired Fecal Occult Blood Tests** - The performance of *FlexSure*<sup>®</sup> *OBT* in an average risk screening population of 1,734 individuals on a restricted diet yielded an apparent specificity for colorectal neoplasia of 98.4% (1,702/1,729) for *FlexSure*<sup>®</sup> *OBT* and 97.2% (1,680/1,729) for Hemocult<sup>®</sup>. For any lower g.i. pathology, the apparent specificity was 99.0% (1,666/1,682) for *FlexSure*<sup>®</sup> *OBT* and 98.8% (1,661/1,682) for Hemocult<sup>®</sup>. The positive predictive value for colorectal neoplasia was 15.6% (5/32) for *FlexSure*<sup>®</sup> *OBT* and 3.9% (2/51) for Hemocult<sup>®</sup>.

#### HIGH RISK POPULATION:

- ◆ **Sensitivity** - The performance of *FlexSure*<sup>®</sup> *OBT* in a high risk population of 283 individuals with a personal or family history of colorectal cancer or adenomas who were on a restricted diet yielded a relative sensitivity for colorectal neoplasia of 55.6% (25/45) for *FlexSure*<sup>®</sup> *OBT* and 51.1% (23/45) for Hemocult<sup>®</sup>. The Negative Predictive Values were not calculated for this group since this parameter is only meaningful in a screening population.

#### STUDIES WITH PRESUMED NORMAL SUBJECTS:

- ◆ **Lower G.I. Specificity** - The apparent specificity (an estimate of specificity due to the inability and inappropriateness of performing colonoscopy on individuals with a negative FOBT result) of *FlexSure*<sup>®</sup> *OBT* for lower gastrointestinal pathology using a group of 88 presumed normal young adults was 97.7% (86/88).
- ◆ **Effect of Diet** - The specificity of *FlexSure*<sup>®</sup> *OBT* for human hemoglobin in 19 presumed normal subjects on restricted, unrestricted, and rare red meat diets was tested. *FlexSure*<sup>®</sup> *OBT* yielded a specificity of 100% regardless of diet.

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STUDIES WITH PRESUMED NORMAL SUBJECTS (continued):

- ◆ **Simulated Upper G.I. Bleeding** - The specificity of *FlexSure*<sup>®</sup> *OBT* for lower g.i. bleeding was studied in a group of presumed normal volunteers who ingested their own blood to simulate upper g.i. bleeding. *FlexSure*<sup>®</sup> *OBT* yielded a specificity of 100% in the four individuals who participated in the study.