

MAR 28 2006

Clinical Micro Sensors, Inc.
eSensor® Cystic Fibrosis Carrier Detection System
Special 510k notification (original 510k ref: k051435)

K060543

eSensor® Cystic Fibrosis Carrier Detection System

510(k) Summary

K060543

510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SDMA 1990 and CFR 807.92.

1. Submitter name, address, contact person and date prepared:

William A. Coty
Clinical Micro Sensors, Inc.
757 South Raymond Ave.
Pasadena, CA 91105
Phone: (626) 463-2000, ext. 8009
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Summary Prepared on February 28, 2006

2. Device Name:

eSensor® Cystic Fibrosis Carrier Detection System

Assay Component:

Device Proprietary/Trade Name: eSensor® Cystic Fibrosis Carrier Detection Kit

Common Name: CFCD Kit

Instrument Component:

Device Proprietary/Trade Name: eSensor® 4800 Instrument

Common Name: 4800 Instrument

3. Legally Marketed Equivalent Device Name

The eSensor® Cystic Fibrosis Carrier Detection System cleared under the 510(k) K051435 is the submitters unmodified legally marketed equivalent device for this Special 510(k) submission.

Note: Under 510(k) submission number K051435 the eSensor® Cystic Fibrosis Carrier Detection System has been determined substantially equivalent to the Tm

Bioscience Tag-It™ Cystic Fibrosis Kit 510(k) K043011, and to the Affymetrix GeneChip® Microarray Instrumentation System 510(k) K003664.

4. Intended Use of the Device

The eSensor® Cystic Fibrosis Carrier Detection (CFCD) System is a device for the detection of carrier status for cystic fibrosis for all adult couples contemplating pregnancy, regardless of ethnicity. It is a qualitative genotyping assay that simultaneously detects mutations currently recommended by the American College of Medical Genetics and American College of Obstetricians and Gynecologists (ACMG/ACOG). The eSensor® CFCD System is not indicated for prenatal screening or for diagnostic purposes, and is for Rx only professional use within the confines of a licensed laboratory, as defined by the Clinical Laboratory Improvement Amendments (CLIA) of 1988.

5. Device Description

The eSensor® Cystic Fibrosis Carrier Detection System is an *in vitro* diagnostic test for the detection and genotyping of a selected panel of 24 cystic fibrosis mutations from DNA isolated from human whole blood.

The CFCD System is a clinical multiplex genetic test system which includes reagents for polymerase chain reaction amplification, exonuclease digestion and hybridization of target DNA, instrumentation and software. The CFCD System uses electrochemical detection to determine the carrier status of patient blood specimens for the ACOG/ACMG recommended panel of 24 cystic fibrosis mutations. Sample preparation for genotyping involves converting each blood specimen into purified genomic DNA (gDNA); then using multiplex PCR amplification followed by exonuclease digestion to convert the gDNA into a set of single-stranded targets. The genotyping reaction is set up with the combination of the single-stranded targets with appropriate buffers containing allele-specific signal probes differentially labeled with electrochemical signaling molecules, called ferrocenes. This mixture is then loaded into cartridges that contain single-stranded capture probes bound to an array of electrodes, with each electrode containing capture probes specific for a single mutation. Cartridges are inserted into the eSensor® 4800 Instrument where the single-stranded targets hybridize to the complementary sequences of the capture probes and signal probes. Detection of the target/probe complexes is achieved using alternating current voltammetry that generates specific electrical signals from the hybridized signal probes. The eSensor® DNA Detection System Application Software then classifies the signals from each mutation and generates a report for each specimen that describes the carrier or non-carrier status of each of the cystic fibrosis panel mutations.

6. Performance Characteristics:

Input DNA Requirements:

Samples containing 10 ng gDNA were tested in the CFCD System. Out of the total of 96 tests, 99.0% gave complete and accurate results, with a lower one-sided 95% confidence bound of 95.1%. Samples containing up to 1,200 ng DNA were tested in method comparison studies and gave accurate results in the CFCD System as compared to DNA sequencing.

Method Comparison:

Per sample: In Clinical Trial Method Comparison studies, 486 samples of freshly collected and banked samples were analyzed using the CFCD System and DNA sequencing. The overall agreement of the CFCD System compared to sequencing was 98.8% (479/486). Omitting samples which failed to give a valid call, agreement between the CFCD System and DNA sequencing was 99.6% (479/481).

Per mutation: Sequencing results were not obtained for 5/7/9T in one sample (an R117H non-carrier). Therefore, using the same data compiled for the per sample calculation above, 11,663 (486 x 24 - 1) individual mutations were analyzed. The overall agreement of the CFCD System compared to DNA sequencing was 98.9% (11,540/11,663). Omitting samples which failed to give a valid result, agreement between the CFCD System and DNA sequencing was 99.97% (11,540/11,543).

Interfering Substances:

The following interfering substances were added separately to whole blood at the concentrations indicated, and no effect was observed on yield of extracted DNA, multiplex amplification of CFTR gene sequences, or genotyping of mutations in the CF carrier panel: triglycerides (3,000 mg/dL), high-density lipoprotein (70 mg/dL), cholesterol (250 mg/dL), bile salts (a mixture of cholate and deoxycholate; 6.4 µg/mL), human albumin (3 g/dL), human immunoglobulin G (3 g/dL), acetaminophen (30 µg/mL), ascorbic acid (30 µg/mL), diphenylhydantoin (phenytoin; 20 µg/mL), gentamicin (12 µg/mL), N-acetylsalicylic acid (200 µg/mL), nicotine (100 µg/mL), theophylline (20 µg/mL), valproic acid (100 µg/mL), vancomycin (100 µg/mL), NaCl (150 mM), KCl (5 mM), CaCl₂ (1.08 mM), FeCl₃ (9.25 µM).

Interfering Mutations:

Δ F508 reflex tests: DNA samples containing the non-disease causing polymorphisms I506V, I507V, and F508C, recommended for testing by the ACMG and ACOG in the event of unexpected homozygosity of Δ F508, have been tested internally with the CFCD System and found to genotype as non-carriers for both Δ F508 and Δ I507. The presence of the F508C polymorphism and the Δ F508 mutation in the same sample did not affect the identification of this sample as a Δ F508 carrier.

Samples heterozygous for the non-panel mutation 2183AA>G are genotyped as carriers for the panel mutation 2184delA. Samples heterozygous for the non-panel mutation R117L will give a "no-call" result for panel mutation R117H.

Reproducibility:

Reproducibility of the CFCD System was determined by testing genomic DNA samples from one non-carrier cell line and 20 carrier cell lines which together expressed all 23 panel mutations. Testing was performed at three sites with three lots of CFCD Assay Kits. Each panel of 21 cell line DNA samples was tested on separate days (5 days per kit lot per site). After re-testing of no-call results, overall per-sample agreement was 99.8%, with a no-call rate of 0.1% and a contradictory call rate of 0.1%. Overall per-mutation agreement was 99.9%, with a no-call rate of 0.1% and a contradictory call rate of 0.008%.

System Failure:

The first-pass no-call rate observed with the CFCD System in the Clinical Trial Method Comparison study of 486 samples was 3.3%, which was reduced to 1.0% after no more than 2 repeat tests for those samples which gave no-call results.

7. Conclusions

The eSensor® Cystic Fibrosis Carrier Detection System accurately identifies a selected panel of mutations in the CFTR gene from genomic DNA isolated from human whole blood.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

MAR 28 2006

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Clinical Micro Sensors, Inc.
c/o William A. Coty, Ph.D.
Vice President, Research and Product Development
757 South Raymond
Pasadena, CA 91105

Re: k060543

Trade/Device Name: eSensor® Cystic Fibrosis Carrier Detection System

Regulation Number: 21 CFR 866.5900

Regulation Name: CFTR (cystic fibrosis transmembrane conductance regulator) gene mutation
detection system

Regulatory Class: Class II

Product Code: NUA

Dated: February 24, 2006

Received: March 1, 2006

Dear Dr. Coty:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

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This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of Compliance at (240) 276-0484. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address <http://www.fda.gov/cdrh/industry/support/index.html>.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Robert L. Becker, Jr.", written in a cursive style.

Robert L. Becker, Jr., M.D., Ph.D.

Director

Division of Immunology and Hematology Devices

Office of In Vitro Diagnostic Device Evaluation and Safety

Center for Devices and Radiological Health

Enclosure

4. **Indications for Use Statement**

INDICATIONS FOR USE STATEMENT

510(k) Number (if known): K060543

Device Name: eSensor® Cystic Fibrosis Carrier Detection System

Indications for Use:

The eSensor® Cystic Fibrosis Carrier Detection (CFCD) System is a device for the detection of carrier status for cystic fibrosis for all adult couples contemplating pregnancy, regardless of ethnicity. It is a qualitative genotyping assay that simultaneously detects mutations currently recommended by the American College of Medical Genetics and American College of Obstetricians and Gynecologists (ACMG/ACOG). The eSensor® CFCD System is not indicated for prenatal screening or for diagnostic purposes, and is for Rx only professional use within the confines of a licensed laboratory, as defined by the Clinical Laboratory Improvement Amendments (CLIA) of 1988.

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use (Per 21 CFR 801.109)

OR

Over-The-Counter Use (Optional Format 1-2-96)

Maria Chan
Division Sign-Off

Office of In Vitro Diagnostic Device
Evaluation and Safety

K060543