

4981341

MAY 22 1998

**PREMARKET NOTIFICATION
510(k) SUMMARY
(As Required By 21 CFR 807.92)**

807.92 (a):

1. Submitter's Name: STC Technologies, Inc.
Address: 1745 Eaton Avenue, Bethlehem, PA 18018
Telephone Number: (610) 882-1820
Contact Person: R. Sam Niedbala, Ph.D., BCFE
Date Prepared: April 8, 1998

2. Device Name:
Proprietary Name: Opiates Micro-Plate EIA (OraSure® Application)
Usual Name: Opiates EIA
Classification Name: Enzyme Immunoassay, Opiates

3. Device to Which Substantial Equivalence Is Claimed:
STC Opiates Micro-Plate EIA (Urine); K924446

4. Description of Device:

Principle of the Assay

The STC Opiates EIA is a competitive micro-plate immunoassay for the detection of opiates in oral fluid collected with the OraSure® Oral Specimen Collection Device. Specimen or standard is added to an EIA well in combination with an enzyme-labeled hapten derivative. In an EIA well containing an OraSure® specimen positive for opiates, there is a competition between the drug and the enzyme-labeled hapten to bind the antibody fixed onto the EIA well. EIA wells are then washed, substrate is added, and color is produced. The absorbance measured for each well at 450 nm is inversely proportional to the amount of opiates present in the specimen or calibrator/control. Because currently there are no SAMHSA assigned cutoffs for opiates testing using oral fluid, STC recommends a cutoff of 10 ng/mL when testing oral fluid collected with the OraSure® Oral Specimen Collection Device. This cutoff is within the limit of detection by the STC Opiates Micro-Plate EIA.

KIT COMPONENTS
Micro-Plate -- Rabbit anti-morphine antibody immobilized on a polystyrene plate supplied in dry form.
Enzyme Conjugate -- Horseradish peroxidase labeled with a morphine hapten diluted in a rotein matrix of bovine serum with protein stabilizers.
Substrate Reagent -- One bottle containing 3,3', 5,5' tetramethylbenzidine.
Stopping Reagent -- Each bottle contains 2 N sulfuric acid.
STC Negative Calibrator -- OraSure [®] Control Matrix negative for morphine.
STC Opiates Negative Control -- OraSure [®] Control Matrix containing 5 ng/mL \pm 3 ng/mL) morphine.
STC Opiates Cutoff Calibrator -- OraSure [®] Control Matrix containing 10 ng/mL (\pm 3 g/mL) morphine.
STC Opiates Positive Control -- OraSure [®] Control Matrix containing 20 ng/mL (\pm 3 g/mL) morphine.

Principle of the OraSure[®] Oral Specimen Collection Device

Saliva is a complex mixture of parotid, submandibular, sublingual and minor salivary gland secretions mixed with mucin, bacteria, leukocytes, sloughed epithelial cells and gingival crevicular fluid. The fact that opiates are present in oral fluid following human use is well documented.⁽²⁾

OraSure[®] was developed for the purpose of collecting oral fluid for diagnostic testing. The collection device consists of a treated absorbent cotton fiber pad affixed to a nylon stick (Collection Pad) and a preservative solution in a plastic container (Specimen Vial). The Collection Pad is impregnated with a mixture of common salts and gelatin which creates a hypertonic environment and an increased osmotic pressure wherever it contacts oral mucosal cells. The pad is placed in contact with the gingival mucosa (between the lower gum and cheek) which enhances the flow of mucosal transudate across the mucosal surfaces onto the absorptive cotton fibers of the pad. Following the collection period, the Collection Pad is placed into a vial containing a preservative solution which serves to inhibit the growth of oral micro-organisms recovered on the Collection Pad. The vial is sealed with a plastic cap and transported to a laboratory for processing and testing. Following processing, a fluid containing a mixture of saliva components and the preservative solution is recovered which is suitable for testing for the presence of opiates in the STC Opiates Micro-Plate EIA manufactured by STC Technologies, Bethlehem, PA. Refer to the OraSure[®] Oral Specimen Collection Device product insert from Epitope for specific instructions on the proper collection, handling, and adequacy of saliva samples.

5. Intended Use Statement

The STC Opiates Micro-Plate EIA is intended for use in the qualitative determination of opiates in oral fluid collected with the OraSure[®] Specimen Collection Device. **For In Vitro Diagnostic Use.**

6. Summary of Technological Characteristics

The STC Opiates Micro-Plate EIA is based on the principle of solid phase competitive enzyme immunoassay . This application is for the modified use of the STC Opiates EIA urine kit for the detection of opiates using specimens collected with the OraSure® Oral Specimen Collection Device manufactured by Epitope, Inc., Beaverton, Oregon. The kit is essentially the same as the predicate urine kit. However, additional standards (supplied with the kit) have been prepared from the OraSure® Specimen Diluent in the OraSure® Collection Device.

807.92 (b):

1. Non Clinical Data

Analytical Sensitivity/Limit Of Detection - The Limit of Detection (LOD) was defined from the signal-to-noise ratio at the zero-drug concentration as the mean zero absorbance (A_0) minus the noise times three ($LOD = A_0 - 3SD$). The LOD was determined by obtaining the absorbance value for twelve blank OraSure® devices and calculating the standard deviation (SD) of the absorbance values. The absorbance value minus 3SD was then extrapolated from the curve and represents the sensitivity of the assay. The LOD was calculated to be 0.2 ng/mL.

Precision - The precision of the STC Opiates Micro-Plate EIA was assessed by testing OraSure® Control Matrix containing 0, 5, 10, or 20 ng/mL morphine. The intra-assay precision was determined by analyzing each level 16 times per run for 4 runs. Inter-assay precision was determined by analyzing 2 samples at each level twice per day for 20 days. The results of this testing are described in the following table:

MORPHINE (ng/mL)	INTRA-ASSAY % CV (n=64)	INTER-ASSAY % CV (n=80/day, 20 days)
0	NA	NA
5	10.4	10.9
10	9.7	9.1
20	12.3	10.8

Analytical Specificity/Cross-Reactivity - The analytical specificity of an immunoassay is defined as the cross-reactivity of substances in the assay which are structurally related to the target compound. The percent cross-reactivity of a compound in the STC Opiates Micro-Plate EIA is defined as the apparent morphine concentration divided by the spiked concentration times 100.

The cross-reactivity of structurally related compounds was calculated at several spiked concentrations in normal human urine. The following table indicates the apparent concentration of morphine for each substance at a concentration which cross-reacted in the assay.

The following compounds cross-react in the assay at the levels shown:

Compound	Tested Concentration (ng/mL)	Morphine Equivalents (ng/mL)	Cross-Reactivity (%)
6-Acetylmorphine	100	14.1	14
Codeine	10	>100	>100
Dextromethorphan	10000	<5	n.d.
Diacetylmorphine	5	10	>100
Hydrocodone	5	33	>100
Hydromorphone	100	79	79
Levorphanol	100	24	24
Meperidine	10000	10	0.1
Morphine	10	10	100
Morphine-3-β-Glucuronide	100	21	21
Nalorphine	1000	11	1.2
Normorphine	1000	7	0.7
Oxycodone	1000	19	1.9
Oxymorphone	10000	51	0.5

*n.d. = not detectable

The following compounds were spiked into OraSure® Control Matrix at a target concentration of 10,000 ng/mL and tested for cross-reactivity. None were found to produce a signal less than or equal to that of the Opiates Cutoff Calibrator.

Acetylsalicylic Acid	Clorazepate	L-Ephedrine	Pentobarbital
Alprazolam	Cocaethylene	L-Methamphetamine	Phenobarbital
Amobarbital	Cocaine	Lidocaine	Phenylephrine
Ampicillin	Cotinine	Medazepam	Phenylpropanolamine
β-Phenethylamine	D-Amphetamine	Methadone	Procainamide
Benzoyllecgonine	D-Methamphetamine	Metroprolol	Procaine
Butabarbital	Fenoprofen	Naproxen	Pseudoephedrine
Butalbital	Gemfibrozil	Niacinamide	Quinidine
Caffeine	Gentisic Acid	Norchlordiazepoxide	Temazepam
Chlordiazepoxide	Glipizide	Nordiazepam	Δ ⁹ -THC
Chlorpromazine	Ibuprofen	PCP	Theophylline
Clonazepam	Imipramine	Penicillin	Zomepirac

It is possible that other substances and/or factors not listed above may interfere with the test and cause false results, e.g., technical or procedural errors.

2. Clinical Data

Accuracy

The clinical sensitivity and specificity of the STC Micro-Plate assay were determined by testing specimens from chronic opiate users. A controlled dose study was also conducted to determine a minimum dose to produce a positive response in the STC EIA. Both studies are described below. The cutoffs for EIA and GC/MS were 10 ng/mL and 15 ng/mL, respectively, for OraSure® specimens. For urine specimens, the EIA cutoff was 300 ng/mL and the GC/MS cutoff was 150 ng/mL (based on SAMHSA recommendations).

Study 1 - Chronic Opiates Users

Matched urine and OraSure[®] specimens were collected from ten (10) self-reported opiates users. An additional fifty (50) presumed negative samples were also included in the analysis. All sixty (60) samples were tested in the STC Opiates Micro-Plate EIA and presumed positives (10) were also tested by gas chromatography/mass spectrometry (GC/MS). Results are presented in the following tables:

Result	OraSure [®] - STC EIA	OraSure [®] - GC/MS*
+	3	2
-	7	8

*Of the 10 samples presumed positive, the % sensitivity and % specificity of the OraSure[®] STC EIA as compared to GC/MS were 100.0% and 87.5%, respectively.

		Urine - STC EIA (300 ng/mL Cutoff)	
		+	-
OraSure [®] -STC EIA (10 ng/mL Cutoff)	+	3	0
	-	4	53

% Relative Sensitivity = 42.9% % Relative Specificity = 100.0%

Result	Urine - STC EIA	Urine - GC/MS**
+	7	8
-	3	2

**Of the 10 samples presumed positive, the % sensitivity and % specificity of the urine STC EIA as compared to GC/MS were 87.5% and 100.0% respectively.

It is believed that the poor agreement between the STC Opiates Micro-Plate EIA (OraSure[®] application) and the STC Opiates Micro-Plate EIA (urine) is driven by differences in the metabolism of heroin and partitioning in oral and urine. Opiates generally appear later in urine and persist for up to 3-6 days.⁽²⁾ Conversely, opiates in saliva is not detectable after 2-8 hours.⁽³⁾ These differences do not diminish the clinical utility of either fluid. However, users should be aware of these differences.

Study 2 - Controlled Dose Study

A total of 5 volunteers in a controlled environment were administered an initial 3 mg of intravenous heroin HCl, followed by a second 6 mg or 12 mg heroin dose 4 to 12 days later. Saliva and urine samples were collected before dosing and periodically for up to 74 hours after dosing. Saliva specimens (400 µL) were added to the collection pad of the OraSure[®] Oral Fluid Collection Device and processed according to the package insert. Samples were then tested using the STC assay and GC/MS.

Using a 10 ng/mL cutoff for OraSure[®] samples, opiates were detectable by EIA for up to 2 hours after a 12 mg heroin dose and not detectable at any time for a 3 or 6 mg dose. Of the GC/MS saliva results, only the initial post-12 mg dose samples contained drug concentrations above the 15 ng/mL LOD/LOQ. This demonstrates the ability of the STC

GC/MS saliva results, only the initial post-12 mg dose samples contained drug concentrations above the 15 ng/mL LOD/LOQ. This demonstrates the ability of the STC EIA to detect opiate concentrations at intravenous doses as low as 12 mg heroin HCl. The ability of the kit to detect opiates at doses between 6 mg-12 mg is unknown.

3. Conclusions

A comparison of the performance data for the new device vs. the predicate device is given on the following page:

STC OPIATES MICRO-PLATE EIA (ORASURE® DEVICE)

PERFORMANCE DATA COMPARISON

1. Limit of Detection

Assay	LOD (ng/mL)
STC Opiates Micro-Plate EIA (Urine)	5.0
STC Opiates Micro-Plate EIA (OraSure®)	0.22

2. Precision

Assay	Intra-Assay % CV Range for Levels Tested	Inter-Assay % CV Range for Levels Tested
STC Opiates Micro-Plate EIA (Urine)	5.5	6.3
STC Opiates Micro-Plate EIA (OraSure®)	8-17	9-13

3. Sample pH Effect

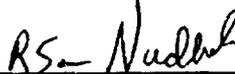
Assay	pH Effect
STC Opiates Micro-Plate EIA (Urine)	No effect pH 3 - 9
STC Opiates Micro-Plate EIA (OraSure®)	False positives at pH ≤ 5.0

4. Effect of Common Materials

Assay	Adulterants Which Affect Assay Results
STC Opiates Micro-Plate EIA (Urine)	Not Tested
STC Opiates Micro-Plate EIA (OraSure®)	Cranberry Juice Orange Juice Cola Cough Syrup

5. Cross-Reactivity

		% Cross-Reactivity in the STC Opiates Micro-Plate EIA	
Compound	Tested Conc. (ng/mL)	OraSure® Assay	Urine Assay, Positive @
6-Acetylmorphine	100	14	500 ng/mL
Codeine	10	>100	75 ng/mL
Dextromethorphan	10000	>0.1	Not Tested
Diacetylmorphine	5	>100	600 ng/mL
Hydrocodone	5	>100	300 ng/mL
Hydromorphone	100	79	600 ng/mL
Levorphanol	100	24	4500 ng/mL
Meperidine	10000	0.1	Not Tested
Morphine-3-β-Glucuronide	100	21	125,000 ng/mL
Nalorphine	1000	1.2	125,000 ng/mL
Normorphine	1000	0.71	125,000 ng/mL
Oxycodone	1000	1.9	125,000 ng/mL
Oxymorphone	10000	0.51	125,000 ng/mL


 R. Sam Niedbala, Ph.D., BCFE
 Executive Vice President



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

MAY 27 1998

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

R. Sam Niedbala, Ph.D.
Executive Vice President
STC Technologies, Inc.
1745 Eaton Avenue
Bethlehem, Pennsylvania 18018-1799

Re: K981341
STC Opiates Micro-Plate EIA
Regulatory Class: II
Product Code: DJG
Dated: April 8, 1998
Received: April 13, 1998

Dear Dr. Niedbala:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to 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). 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 (Premarket Approval), 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 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

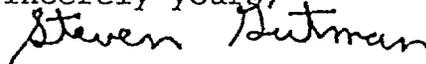
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Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770) 488-7655.

This letter will allow you to begin marketing your device as described in your 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 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "<http://www.fda.gov/cdrh/dsmamain.html>".

Sincerely yours,



Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

STATEMENT OF INDICATIONS FOR USE

510(k) Number (if known): K981341

Device Name: STC Opiates Micro-Plate EIA

Indications For Use: The STC Opiates Micro-Plate EIA is intended for use in the qualitative determination of opiates in oral fluid collected with the OraSure® Oral Collection Device. For In Vitro Diagnostic Use.

(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 _____

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Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K981341