OraSure® HIV-1 Oral Specimen Collection Device

A device for the collection of oral fluid specimens for detection of antibodies to Human Immunodeficiency Virus Type 1 (HIV-1)

IV **For *In Vitro* Diagnostic Use**

NAME AND INTENDED USE

OraSure HIV-1 Oral Specimen Collection Device is intended for use in the collection of oral fluid specimens by properly trained individuals for the purpose of testing for the presence of antibodies to Human Immunodeficiency Virus Type 1 (HIV-1). OraSure HIV-1 specimens are intended to be used only with the Avioq HIV-1 Microelisa System screening test manufactured by Avioq, Inc. OraSure HIV-1 is intended for use with subjects 13 years of age or older.

RESTRICTIONS

- Specimen collection must be performed under the supervision of trained personnel, i.e., a person trained in the use of the collection device.
- Test subjects must receive the pamphlet entitled "Subject Information" prior to specimen collection.
- Testing of OraSure HIV-1 oral fluid specimens for HIV-1 antibodies is restricted to testing with the Avioq HIV-1 Microelisa System screening test manufactured by Avioq, Inc.
- The OraSure HIV-1 device is restricted to use for diagnostic purposes and must not be used to screen blood donors.

NOTE: See "Warnings," "Precautions" and "Directions for Use" sections for information on:

1) Reduced sensitivity of testing with OraSure HIV-1 specimens compared with testing of blood specimens.
2) Provision of the "Subject Information" pamphlet to subjects prior to specimen collection.

SUMMARY AND EXPLANATION OF THE ORASURE HIV-1 COLLECTION DEVICE

Early experience using oral fluid for HIV-1 testing suggested that there was a problem of specimen instability and assay insensitivity (see "Analytical Sensitivity" section). 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. Gingival crevicular fluid, or mucosal transudate, is the fluid derived from the passive transport of serum components through the oralmucosa into the mouth. Among the serum components in mucosal transudate are immunoglobulins or antibodies. Antibodies that are specific for the HIV virus can be detected by ***in vitro*** tests.

The OraSure HIV-1 device consists of an absorbent cotton fiber pad, impregnated with a proprietary mixture of common salts and gelatin, affixed to a nylon stick. The pad creates a hypertonic environment and an increased osmotic pressure whenever it contacts oral mucosal cells. The pad is placed in contact with the gingival mucosa (between the lower gum and cheek) and enhances the flow of mucosal transudate across the mucosal surfaces onto the absorptive cotton fibers of the pad.

Oral fluid contains a number of enzymes (proteases) which degrade oral bacteria and proteins, including antibodies. Specimens collected from the mouth must be preserved to ensure that the antibodies are intact when the specimens arrive at the laboratory for testing. The OraSure HIV-1 device includes preservatives that are effective in protecting antibodies from degradation.

PRINCIPLE OF THE PROCEDURE

Prior to the specimen collection, each subject must be given the "Subject Information" pamphlet provided with each device and counseled about 1) HIV antibody testing using the OraSure HIV-1 device, 2) the alternative of giving a blood specimen, 3) HIV-1 risks and 4) HIV-1 antibody testing.

The OraSure HIV-1 device consists of a treated absorbent cotton fiber pad affixed to a nylon stick and a preservative solution in a plastic container. Under the supervision of the trained personnel, the specimen is collected by the subject rubbing the pad between his/her lower gum and cheek until moist, and then leaving the pad stationary for a minimum of two minutes (time verified by the trained personnel). The cotton pad contains salts and gelatin which facilitate the flow of antibodies from the gingival mucosa into the mouth and onto the pad. The subject then promptly places the pad in a vial containing a preservative solution which stabilizes HIV antibodies. The vial is then capped by the collector and transported to a qualified laboratory for testing.

At the laboratory, the specimen is processed for testing with the Avioq HIV-1 Microelisa System. The laboratory will measure the volume of the specimen to determine that a minimum volume of specimen was collected. If a *minimum* volume of specimen was not collected, the specimen is unsuitable for testing and a new specimen from the test subject must be obtained.

Following performance of the EIA test, the results of the test will be reported to a physician or third party.

MATERIAL PROVIDED WITH EACH DEVICE (REF 3001-2871)

1. One treated cotton fiber Collection Pad (contains gelatin) on a nylon stick (REF 3001-0868).
2. One Specimen Vial containing blue preservative solution (REF 3001-0869).
3. "Subject Information" pamphlet.

MATERIALS REQUIRED BUT NOT PROVIDED

1. Timer capable of timing 2 minutes.
2. If oral fluid specimens are not collected from subjects in a medical setting, the trained collector should be provided with sealable containers to safely handle the specimens; for example, sealable pastic bags of 2 mil thickness.
3. Additional materials may be required to protect the OraSure HIV-1 Specimen Vials from impact, direct sunlight, and temperatures exceeding 37°C (98°F) during transport; for example, styrofoam containers or insulated coolers and cold packs.

⚠ WARNINGS

1. HIV-1 antibody testing of OraSure HIV-1 specimens has reduced sensitivity compared with HIV-1 antibody testing of blood specimens (see "Performance Characteristics" section for details).
2. Studies to determine the performance characteristics of the OraSure HIV-1 device in subjects younger than 18 years of age have not been performed.
3. This device is not intended to collect saliva *per se*. Failure to carefully follow the collection procedure may cause erroneous results.
4. Testing laboratories will not test a specimen of insufficient volume.

PRECAUTIONS

1. OraSure HIV-1 Specimen Vials are breakable and should be handled with care.
2. OraSure HIV-1 specimens should not be exposed to temperatures to exceeding 37°C (98°F) or direct sunlight.
3. Handle specimens and materials contacting specimens as if potentially infectious biological materials in accordance with "Universal Precautions for Prevention of Transmission of Human Immunodeficiency Virus, Hepatitis B Virus, and Other Blood-borne Pathogens in Health-Care Settings" (CDC, MMWR, June 24, 1988). It has been reported that infectious HIV can be isolated from the oral fluid of some infected patients. When detectable in oral fluid, infectious virus is present at low levels compared with blood and may be inactivated by salivary inhibitors.
4. Occupational Safety and Health Administration (OSHA) regulations apply to personnel collecting and handling specimens.
5. Federal, state and local regulations for human biologic test specimens apply to the transportation of OraSure HIV-1 oral fluid specimens which may contain etiologic agents.
6. Use freshly prepared 10% bleach to decontaminate surfaces in the event of a spill of a collected specimen.
7. Avoid contamination of collection device and the Specimen Vial solution with foreign matter.
8. Do not use the Collection Pad if the package has been opened.
9. Do not touch the Collection Pad with fingers before or after specimen collection.
10. Do not use if the Collection Pad is wet.
11. Do not use device beyond expiration date shown on the device package.

STORAGE OF UNUSED ORASURE ORAL SPECIMEN COLLECTION DEVICES

Store unused OraSure Oral Specimen Collection Devices at room termperature (18-25°C/64-77°F, not to exceed 37°C/98°F). Exposure to higher temperatures should be avoided. Protect from prolonged exposure to direct sunlight.

DIRECTIONS FOR USE

1. Prior to specimen collection, please read "Subject Information" pamphlet. This pamphlet cotains information about OraSure, HIV, and AIDS. If the subject cannot read the pamphlet, the information should be read to the subject. The subject should be informed of other options for HIV testing, including blood tests and encouraged to ask questions. Subjects should be provided this package insert upon request.
2. Open the outer OraSure HIV-1 package containing the Collection Pad and the Specimen Vial.
3. To open the Collection Pad package, orient the package so that the pad is "down" and the "stick" end is up.
4. With the thumb and index finger of each hand, simultaneously peel and symmetrically peel apart the two sides of the packaging far enough to allow easy removal of the Collection Pad.
5. Instruct the subject to take the stick of the device and pull the Collection Pad out of the packaging sleeve.
6. Instruct the subject to place the Collection Pad inside the mouth (pad oriented down) between the lowercheek and gum and gently rub the pad back and forth along the gum line until the pad is moist.
7. Begin timing for two (2) minutes.
8. Instruct the subject to leave the pad stationary against the lower gum for a minimum of two (2) minutes, and a maximum of five (5) minutes.
9. Instruct the subject to remove the Specimen Vial from the package and record identification information and date of collection on the Specimen Vial.
10. Instruct the subject to open the vial in an upright position (with the cap up, pointed tip down) by gently rocking the cap back and forth to avoid spilling the contents.
11. At the end of two minutes, instruct the subject to remove the pad from the mouth and insert the pad into the blue liquid at the bottom of the Specimen Vial, and push the pad all the way to the bottom of the vial.
12. Instruct the test subject to break the plastic shaft of the device by bending it against the side of the vial. (the shaft is scored to facilitate breakage.)

13. Instruct the subject to place the cap onto the vial, ensuring a tight fit. The cap will "snap" into place when secure.
14. For specimens collected outside of a medical setting, secure the specimen vial in the sealable container provided by the ordering physician or the trained personnel (see "Materials Required But Not Provided" section).
15. Follow the instructions of the ordering physician or the trained personnel for handling collected specimens.

CAUTION: Protect vials of OraSure HIV-1 specimens from impact, direct sunlight and temperatures exceeding 37°C (98°F) as described in "Materials Required But Not Provided" section.

STORAGE AND TRANSPORTATION OF ORASURE HIV-1 SPECIMENS TO THE TESTING LABORAORY

1. Collected specimens must be stored and transported in the OraSure HIV-1 Specimen Vial.
2. Collected specimens should be protected from impact, direct sunlight and temperatures exceeding 37°C (98°F).
4. Prior to sending OraSure HIV-1 specimens to a testing laboratory, verify that the testing laboratory is qualified to test OraSure HIV-1 specimens using the Avioq HIV-1 Microelisa System manufactured by Avioq, Inc.
5. Federal, state and local regulations regarding transportation of etiologic agents are applicable to OraSure HIV-1 specimens.

ORASURE HIV-1 SPECIMEN TEST PROCEDURE

Refer to the Avioq HIV-1 Microelisa System package insert specimen processing instructions and testing procedures.

RESULTS

Test results may be obtained only by the ordering physician or someone under his/her supervision from a laboratory performing the Avioq HIV-1 Microelisa System manufactured by Avioq.Inc.

INTERPRETATION OF RESULTS

In providing test results to subjects, careful note must be taken of the limitations of the procedure (see following section.)

NEGATIVE RESULTS: OraSure HIV-1 specimens that are nonreactive in the Avioq HIV-1 Microelisa System are considered negative for antibodies to HIV-1.

POSITIVE RESULTS: OraSure HIV-1 specimens that are repeatedly reactive by the Avioq HIV-1 Microelisa System must be confirmed by a confirmatory test.

LIMITATIONS OF THE PROCEDURE

1. Subjects must be counseled that false negative results occur more frequently when testing with OraSure HIV-1 specimens compared with testing blood specimens. (See "Performance Characteristics of the Test for OraSure HIV-1 Specimens").
2. Studies to determine the performance characteristics of the OraSure HIV-1 Oral Specimen Collection Device in subjects younger than 18 years of age have not been performed.
3. False results (either positive or negative) may occur as a result of interfering substances being collected with the specimen.
4. False negative results (the subject is infected, but OraSure HIV-1 is negative) may occur as a result of the absence of antibodies to HIV-1 in the early phase of the infection, or anti-HIV levels which are below the lower limit of detection of this procedure.
5. False positive results may occur, for example, as a result of nonspecific cross reacting antibodies, and not from an HIV-1 infection.
6. A person who has antibodies to HIV-1 is presumed to be infected with the virus, except that a person who has participated in an HIV vaccine study may develop antibodies to the vaccine and may or may not be infected with HIV. Clinical correlation is indicated with appropriate counseling, medical evaluation, and possibly additional testing to decide whether a diagnosis of HIV infection is accurate.

PERFORMANCE CHARACTERISTICS OF THE TEST FOR ORASURE HIV-1 SPECIMENS

Summary of Sensitivity and Specificity of Testing OraSure HIV-1 Specimens
Non-Inferiority Study

A small non-inferiority study was performed between Avioq HIV-1 Microelisa System and the licensed comparator Oral Fluid Vironostika® HIV-1 Microelisa System. The study indicated that the Avioq HIV-1 Microelisa System was not inferior to that of the licensed comparator Oral Fluid Vironostika® HIV-1 Microelisa System.

ORIGINAL ORAL FLUID PERFORMANCE CHARACTERISTICS

All Performance Characteristics presented below are from the licensed Oral Fluid Vironostika® HIV-1 Microelisa System.

Sensitivity and specificity

At present, there is no recognized standard for establishing the presence or absence of HIV-1 antibody in human oral fluid. Therefore, sensitivity testing of OraSure HIV-1 specimens with the Oral Fluid Vironostika® HIV-1 Microelisa System was computed based on the clinical diagnosis of AIDS and specificity was computed based on testing in low risk populations. In addition, sensitivity and specificity of OraSure HIV-1 testing were computed based on testing in high risk subjects using matched oral fluid/blood from the same subject specimens for comparison.

1. Sensitivity using OraSure HIV-1 was reduced compared with blood specimens based on an assumed 100% prevalence of HIV-1 antibody in AIDS patients:

   Sensitivity using OraSure HIV-1 specimens with the Oral Fluid Vironostika® HIV-1 Microlelisa System was estimated from clinical studies to be 98.6% (287/291) for AIDS patients.

   Sensitivity using OraSure HIV-1 was reduced compared with blood specimens for high risk subject based on the ability of the test to detect HIV-1 antibodies in paired blood and OraSure HIV-1 speciments:

   Sensitivity using OraSure HIV-1 specimens with the Oral Fluid Vironostika® HIV-1 Microlelisa System was estimated in clinical studies to be 99.1% (546/551) for high risk subjects.

2. Specificity using OraSure HIV-1 specimens with the Oral Fluid Vironostika® HIV-1 Microelisa System was reduced compared with blood specimens in low risk populations based on an assumed zero prevalence of HIV-1 antibody, and was estimated from clinical studies to be 99.6% (3991/4009).

   Specificity using OraSure HIV-1 specimens with the Oral Fluid Vironostika® HIV-1 Microelisa System was reduced compared with blood specimens in seronegative high risk populations, and was estimated from clinical studies to be 97.7% (837/857).

Oral Fluid Vironostika® Microelisa System (ELISA) Clinical Trial:

A total of 5720 matched OraSure and serum specimens were collected at seven sites (see following table) from AIDS patients, high risk subjects and low risk subjects 18 years and older. The high risk subjects were composed of injection drug users (38%), homosexuals (23%), sexual partners of individuals at risk (17%), prostitutes (6%), and others with acknowledged risk factors (16%). The low risk population consisted of (55%) military inductees, (16%) blood donors, (14%) insurance applicants, and (11%) students/hospital staff. The performance of the Oral Fluid Vironostika® HIV-1 Microelisa System was evaluated by comparing OraSure ELISA results to the matched serum specimens tested with a licensed HIV-1 ELISA and Western Blot.

Table 1. Clinical Trial Sites and Populations

Test Site	AIDS Subjects	High Risk Subjects	Low Risk Subjects
A	11	407	84
B	0	466	0
C	158	299	1,132
D	65	240	104
E	57	0	336
F	0	0	573
G	0	0	1,788
Total	291	1,412	4,017

ELISA Sensitivity

Reactivity in AIDS patients and high risk populations: The sensitivity of testing OraSure HIV-1 specimens compared with matched serum specimens using the Oral Fluid Vironostika® HIV-1 Microelisa System in AIDS patients and high risk subjects (38% intravenous drug users, 23% homosexuals, 17% sexual partners of individuals at risk, 6% prostitutes, 16% others with acknowledged risk factors) is shown in Table 2.

Table 2. Reactivity in AIDS Patients and High Risk Populations

	No. of Specimens	Nonreactive[a] No.	Reactive No.	Confirmed Positive with Serum No.
AIDS Patients				
OraSure	291	4[b]	287	
Serum	291	1	290	291
High Risk Subjects				
OraSure	1,412	843[c]	569[d]	
Serum	1,412	858	554[e]	551

a. Includes specimens that were nonreactive on the initial screening test and specimens that were initially reactive, but not repeatedly reactive.

b. 4 matched serum specimens were reactive (**OraSure HIV-1 False Negative**). Screening tests for 2 patients were valid by ELISA kit criteria and the matched serum specimens were reactive with S/CO of 7.26 and 6.90, but laboratory control reagents failed. Retests of these OraSure HIV-1 specimens at the clinical site were reactive for both specimens with S/CO values of 1.69 and 1.15.

c. 5 matched serum specimens were reactive (**OraSure HIV-1 False Negative**).

d. 20 matched serum specimens were nonreactive (**OraSure HIV-1 False Positive**); 3 OraSure HIV-1 specimens were ELISA initially reactive and not retested and matched serum specimens were negative (**OraSure HIV-1 Unresolved**).

e. 2 subjects tested blood Western Blot negative (**Blood False Positive**); 1 subject was ELISA initially reactive, not retested and Indeterminate by blood Western Blot (**Unresolved**).

ELISA = Oral Fluid Vironostika® Microelisa System assay; S/CO = signal to cutoff

287 OraSure HIV-1 specimens (98.6%) and 290 matched serum specimens (99.7%) were reactive in the Oral Fluid Vironostika® HIV-1 Microelisa System screening test out of the 291 AIDS patients studied. Of the four OraSure HIV-1 specimens that were initially nonreactive, one was nonreactive when retested and three were reactive when retested. One serum specimen that was initially nonreactive was reactive when retested.

546 OraSure HIV-1 specimens (99.1%) and 551 matched serum specimens (100%) were reactive in the Oral Fluid Vironostika® HIV-1 Microelisa System screening test out of the 551 high risk subjects whose serum tested positive in additional, more specific tests for HIV-1 antibodies (Western Blot, radioimmunoprecipitation assay (RIPA)). Of the five OraSure HIV-1 specimens that were initially nonreactive, two were repeatedly nonreactive on ELISA retest, two were not retested and one was repeatedly reactive on retest.

The sensitivity of testing OraSure HIV-1 specimens with the Oral Fluid Vironostika® HIV-1 Microelisa System compared with matched serum specimens was reduced based on the reactivity in AIDS patients and high risk subjects.

Analytical Sensitivity: The analytical sensitivity of testing OraSure HIV-1 specimens with the Oral Fluid Vironostika® HIV-1 Microelisa System was 1/1000th that of testing serum specimens based on serial dilution of matched specimens from 13 HIV-1 antibody positive subjects. At the dilutions recommended for testing, 1:2 for OraSure HIV-1 specimens and 1:75 for serum specimens, the average sensitivity of testing with OraSure HIV-1 specimens was 1/35th (range 1/7 to 1/107) of the matched serum specimens based on the highest dilution producing positive results as shown in Table 3.

Table 3. Highest Dilution Yielding Reactive ELISA Results

Specimen Number[a]	OraSure Titer[c]	Serum Titer[c]	OraSure Hemoglobin[b] (mg/dL)
1	128	4096	
2	128	4096	
3	64	4096	
4	64	1024	
5	128	4096	
6	128	4096	
7	128	4096	
8	512	4096	
9	128	4096	
10	512	4096	
11	160	17067	11.0
12	1280	8533	7.6
13	160	8533	5.3

a. Paired specimens 1-10 were collected for analytical study. Paired specimens 11-13 were collected as part of the clinical field trial.

b. Three OraSure HIV-1 specimens (#11-13) of 112 studied contained hemoglobin (>5mg/dL).

c. End-point titer indicates the maximum dilution of a specimen (prior to dilution for ELISA testing) which produced reactive Oral Fluid Vironostika® HIV-1 Microelisa System test results.

The analytical sensitivity of Oral Fluid Vironostika® HIV-1 Microelisa System for HIV-1 antibodies in three OraSure HIV-1specimens was not enhanced by the presence of hemoglobin in the OraSure HIV-1 specimens.

Reactivity in Seroconversion: OraSure HIV-1 and serum specimens were obtained prospectively from one subject undergoing seroconversion. ELISA results showed HIV-1 antibodies were detected in serum specimens on day 8 and in the OraSure HIV-1 specimens on day 11 based on two consecutive reactive determinations. ELISA results of serum and OraSure specimens and results of serum Western Blot and HIV-1 antigen testing on serum are summarized in Table 4.

Table 4. ELISA, Serum Western Blot, and HIV-1 Antigen Test Results of OraSure HIV-1 and Serum Specimens from a Single Subject Undergoing Seroconversion

Date	(Day)	OraSure S/CO	Serum S/CO	Serum p24 Ag (ng/mL)	Serum Western Blot band reactivity					
5/14	(1)	0.36	0.40	13.64*	none					
5/15	(2)	0.57								
5/16	(3)	0.31	0.40	20.36*	none					
5/17	(4)	0.52								
5/21	(8)	0.49	2.92*	6.43*	gp160±	p24±*				
5/22	(9)	1.07*								
5/23	(10)	0.96	4.71*	1.92*	gp160±	p24+	gp41±*			
5/24	(11)	1.75*								
5/28	(15)	1.94*	5.26*	0	gp160+	p24+	gp41±	gp120±*		
5/29	(16)	2.05*								
5/30	(17)	2.04*	5.27*	0	gp160+	p24+	gp41±	gp120±*		
5/31	(18)	2.04*								
6/4	(22)	1.91*	5.44*	0	gp160+	p24+	gp41±	gp120±	p65±	p55±*

*Asterisk indicated a reactive test result; S/CO = signal to cutoff; Ag = HIV-1 antigen; + = present; ± = indeterminate

Reactivity in Seropositive Subjects with Oral Pathology: Oral examinations were carried out at clinical site D on 65 AIDS sugjects, 240 high risk subjects and 18 subjects of unknown risk. Of the 303 subjects found to be seropositive, 29 (10%) had significant oral pathology. For these subjects HIV-1 antibodies were detected in 96.6% (28/29) of the OraSure speciments and 100% (29/29) of the serum specimens when tested using the Oral Fluid Vironostika® HIV-1 Microelisa System as show in Table 5.

Table 5. OraSure HIV-1 ELISA and Serum Western Blot for Seropositive Subjects with Oral Pathology

Oral Pathology	Number Tested	Number OraSure ELISA Reactive	Number Confirmed Positive with Serum Blot
Hairy leukoplakia	10	10	10
Candida	10	9[a]	10
Gingivitis	5	5	5
Gingival ulcer	1	1	1
Periodontitis	1	1	1
Hairy leukoplakia and candida	1	1	1
Hairy leukoplakia and gingivitis	1	1	1
Total	29	28	29

a. Includes one **OraSure HIV-1 false negative** which was previously noted in high risk populations.

This study did not detect an increase in the frequency of false negative results for OraSure HIV-1 specimens obtained from subjects with the above oral pathologies.

ELISA Specificity

The specificity of testing OraSure HIV-1 specimens with the Oral Fluid Vironostika® HIV-1 Microelisa System compared with testing serum specimens was studied in 4,017 low risk subjects (55% military inductees, 16% blood donors, 14% insurance applicants, 11% students/hospital staff) and 1,412 high risk subjects. The results are shown in Table 6.

Table 6. Summary of ELISA Testing of Low and High Risk Populations

	No. Specimens	Nonreactive[a] No.	Reactive	Confirmed Positive with Serum No.
Low Risk Subjects				
OraSure	4,017	3,992	25[b]	
Serum	4,017	4,008	9[c]	4
High Risk Subjects				
OraSure	1,412	843	569[d]	
Serum	1,412	858	554[e]	551

a. Includes specimens that were nonreactive on initial screening test and specimens that were initially reactive, but not repeatedly reactive.

b. 18 matched serum specimens were negative **(OraSure HIV-1 False Positive)**; 3 OraSure HIV-1 specimens were initially reactive by ELISA and not retested and matched serum specimens were ELISA nonreactive and blood Western Blot Indeterminate **(Unresolved)**.

c. 4 specimens were confirmed negative **(Blood False Positive)**; 1 specimen was ELISA repeatedly reactive, but not tested further **(Unresolved)**.

d. 20 matched serum specimens were negative **(OraSure HIV-1 False Positive)**; 3 matched serum specimens were negative and OraSure HIV-1 was ELISA initially reactive and not retested. 19 of the 20 subjects with false positive OraSure HIV-1 results were smokers.

e. 2 specimens were blood Western Blot Negative **(Blood False Positive)**; 1 specimen was ELISA initially reactive and blood Western Blot Indeterminate **(Unresolved)**.

There were 18 repeatedly reactive OraSure HIV-1 specimens (18/4009, 0.45%) compared with 4 repeatedly reactive serum specimens (4/4009, 0.10%) in the low risk subjects whose HIV antibody status was resolved to be negative by additional testing. There were 20 repeatedly reactive OraSure HIV-1 specimens (20/857, 2.3%) compared with 2 repeatedly reactive serum specimens (2/860, 0.23%) in the high risk subjects whose antibody status was resolved to be negative by additional testing.

These results suggest that, compared with testing serum specimens, the incidence of false repeatedly reactive test results using OraSure HIV-1 specimens is increased 4.5-fold in low risk populations and 10-fold in high risk populations.

Reactivity in Subjects with Other Disease Conditions: Thirty-eight (38) repository and 53 fresh paired OraSure HIV-1 and serum specimens from patients with medical conditions other than HIV-1 infection were studied. ELISA results of OraSure HIV-1 and serum specimens were negative in all cases as presented in Table 7.

Table 7. ELISA Results for Subjects with Medical Conditions other than HIV-1 Infection

Disease	Number Tested	Number Reactive	Number Negative
Hepatitis A	12	0	12
Hepatitis B	5	0	5
Hepatitis C	18	0	18
Autoimmune	13	0	13
H. pylori	3	0	3
Lymphoid malignancy	16	0	16
Other neoplasia	24	0	24
Total	91	0	91

Reactivity in Seropositive Subjects with Oral Pathology: Paired OraSure HIV-1 and serum specimens were obtained prospectively from 47 subjects with various forms of oral pathology. Results of testing OraSure HIV-1 and serum specimens with Oral Fluid Vironostika® HIV-1 Microelisa System were negative in all cases as presented in Table 8.

Table 8. ELISA Results for Seronegative Subjects With Oral Pathology

Oral Pathology	Number Tested	Number Positive	Number Negative
Periodontitis	21	0	21
Gingivitis	5	0	5
Multiple caries	5	0	5
Multiple caries and periodontitis	8	0	8
Multiple caries and gingivitis	6	0	6
Periodontitis and gingivitis	2	0	2
Total	47	0	47

This study did not detect differences in specificity among the OraSure HIV-1 specimens obtained from subjects with the oral pathology noted above when tested in the Oral Fluid Vironostika® HIV-1 Microelisa System.

ELISA Reproducibility

The reproducibility results of testing OraSure HIV-1 specimens in the Oral Fluid Vironostika® HIV-1 Microelisa System are presented in Table 9.

Table 9. ELISA Results for OraSure Specimens Tested at 3 Sites

Specimen No.	Mean S/CO	%CV	Test n	Test Days	Test Location A	B	OTI
1	6.046	2.3	36	2	X		
2	6.018	2.4	36	2	X		
3	5.933	5.9	33	2	X		
4	6.142	2.6	5	2	X		
5	2.852	10.6	24	3		X	X
6	1.639	29.6	10	3	X	X	
7	0.422	23.7	82	3	X	X	
8	0.299	14.4	88	3	X	X	

OraSure HIV-1 specimens from four seropositive subjects (specimens 1-4) and two seronegative subjects (specimens 7 and 8) were collected at two test sites. Specimens collected at one clinical site were tested on-site and exchanged with the other site for testing where indicated. OraSure HIV-1 specimens from two seropositive subjects were collected and diluted at OTI to provide one intermediate (specimen 5) and one low positive specimen (specimen 6) for testing. Specimens prepared at OraSure Technologies were sent to clinical sites for testing and/or tested at OTI as indicated.

Additional ELISA Performance Studies

The performance of OraSure HIV-1 specimens collected by trained medical professionals and trained non-medical individuals compared with matched serum specimens were evaluated using the Oral Fluid Vironostika® HIV-1 Microelisa System. Paired OraSure HIV-1 and serum specimens were obtained from 129 subjects prospectively and the results of testing are presented in Table 10.

Table 10. ELISA Results for Specimens Collected by Trained Medical Professionals and Trained Non-Medical Persons or Individuals

Type of Collector	Type of Specimen	ELISA Nonreactive	ELISA Reactive
Medical professional	OraSure	94	35[a]
Non-medical	OraSure	95	34[b]
Medical professional	Serum	96	35[c]

a. 3 matched sera were nonreactive **(OraSure HIV-1 False Positive)**.

b. 2 matched sera were nonreactive **(OraSure HIV-1 False Positive)** and coincided with these identified in footnote a. above.

c. One serum was reactive by ELISA and Indeterminate by blood Western blot [p65+] **(Unresolved)**.

Reactive ELISA results for OraSure HIV-1 specimens collected by trained medical professionals and non-medical individuals from 32 subjects were concordant with serum results. One subject had discordant results; the OraSure HIV-1 specimen was ELISA repeatedly negative and serum specimen was ELISA repeatedly reactive and Western Blot indeterminate with p65 reactivity. There was no follow up testing to resolve the true serostatus of this subject.

Three OraSure HIV-1 specimens collected by medical professionals and two OraSure HIV-1 specimens collected by non-medical individuals were repeatedly reactive on the ELISA test while matched serum specimens were negative on ELISA and Western Blot tests (OraSure HIV-1 false positive).

In this study, the performance of ELISA testing of OraSure HIV-1 specimens collected by trained non-medical individuals was comparable to OraSure HIV-1 specimens collected by medical professionals.

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[Note: If you want additional copies of this document you can obtain them free-of-charge by calling OraSure Technologies at 1-800-869-3538. You are also welcome to make copies of this document yourself.]

EXPLANATION OF SYMBOLS

	Avoid Prolonged Exposure to Direct Sunlight		Do Not Reuse
LOT	Batch Code	IVD	*In Vitro* Diagnostic Medical Device
REF	Catalog Number		Manufacturer
	Caution, Consult Accompanying Documents		Temperature Limitation
	Consult Instructions for Use		Use By
CALIBRATOR	Calibrator	PACK INSERT	Package Insert
COL DEVICE	Collection Device	PN	Part Number
COLLECT DATE	Collection Date		Protect from Impact
CONTENTS	Contents	SUBJ ID#	Subject ID#
CONTROL	Control	OSCD	Oral Speciment Collection Device
DISTRIBUTED	Distributed By	ORAL SPEC VIAL	Oral Specimen Vial
PEEL OPEN HERE	Peel Open Here	EC REP	Authorized Representative in the European Community

OraSure Technologies, Inc.

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Bethlehem, PA 18015
Made in USA
(610) 882-1820 In the USA
(001) 610-882-1820 Outside the USA

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