OraSure® HIV-1 Western Blot Kit
Summary of Safety and Effectiveness

I. General Information

PMA Number:	BP950004
Trade Name:	OraSure® HIV-1 Western Blot Kit
Generic Name:	Human Immunodeficiency Virus - Type I Western Blot Kit
Applicant:	Epitope, Inc. 8505 SW Creekside Place Beaverton, OR 97008
Date of Notice of Approval:	

II. Indications for Use

The OraSure HIV-1 Western Blot Kit is an *in vitro* qualitative assay for the detection of antibodies to individual proteins of the Human Immunodeficiency Virus Type 1 (HIV-1) in human oral fluid specimens obtained with the OraSure HIV-1 Oral Specimen Collection Device. It is intended for use as an additional, more specific test for HIV-1 antibodies in OraSure specimens collected from individuals of unknown risk for HIV-1 which are found to be repeatedly reactive by the Oral Fluid Vironostika® HIV-1 Microelisa System. The OraSure HIV-1 Western Blot Kit is intended for professional use only.

The OraSure HIV-1 Western Blot Kit is not intended for use with blood, serum/plasma or urine specimens, or for screening or reinstating potential blood donors.

III. Device Description

A. Description of the Kit

The OraSure HIV-1 Western Blot Kit has been developed by modification of the serum-based HIV-1 Western Blot Kit, manufactured by Epitope, Inc. under U.S. License #1133. The OraSure test kit manufacturing processes and assay procedures rely upon the same chemical and biological principles employed by the currently licensed kit. The primary modifications adopted for testing of oral specimens are the inclusion of a goat anti-human antibody possessing only the $F(ab')_2$ fragment rather than whole antibody; an alkaline phosphatase-BCIP/NBT color development system rather than the horseradish peroxidase 5-amino-indole system; and extended incubation times. In addition, the HIV-1 viral lysate used as antigen undergoes an initial tangential

filtration (Prostak™, Millipore, Inc.) rather than a settling-out process during purification from cell culture.

Components of the test kit are:

- OraSure HIV-1 Western blot strips: Prenumbered nitrocellulose strips; preblotted with resolved HIV-1 viral proteins; packed in a resealable plastic pouch between buffer-soaked absorbent paper; buffer containing 0.1% sodium azide as a preservative.
- Substrate: BCIP/NBT single reagent substrate in an organic base/TRIS buffer.
- Powdered Milk: Non-fat milk solids.
- Sample Diluent Concentrate: Phosphate buffered saline with 3.0% Tween-20; contains 0.01% thimerosal (once diluted) as a preservative.
- Conjugate Concentrate: Goat anti-human IgG (heavy and light chain specific) $F(ab')_2$ fragment, labeled with alkaline phosphatase; contains 0.1% sodium azide as a preservative.
- OraSure HIV-1 WB Negative Control: Human serum or plasma, non-reactive for antibodies to HIV-1, in OraSure Control Matrix; tested negative for HBsAg and antibody to HCV.
- OraSure HIV-1 WB High and Low Positive Controls: Human serum or plasma, reactive for antibodies to HIV-1, in OraSure Control Matrix; tested negative for HBsAg and antibodies to HCV; heat-inactivated to render material noninfectious for HIV-1.

B. Principles of the Test

OraSure HIV-1 specimens, diluted in Sample Buffer (1:10 dilution of Sample Diluent Concentrate with 3.0% Powdered Milk), are incubated with the preblotted nitrocellulose strips. If antibodies to specific HIV-1 proteins are present in a specimen, they bind to epitopes contained in the proteins banded on the strip. Any antibody not bound is removed by washing. The conjugate is then added to the strip and allowed to incubate. It binds to antibodies already bound to viral proteins on the strip. Excess conjugate is removed by washing. The strips are then incubated with substrate. The color reaction is stopped by aspiration and washing.

If antibodies to specific HIV-1 proteins (p) or glycoproteins (gp) are present in the specimen in sufficient concentration, purple bands may be visible at one or more of the following positions on the nitrocellulose strip: gp160, gp120, p65, p55, p51, gp41, p31, p24 and p18 (number refers to apparent molecular weight in kilodaltons).

C. Manufacturing

All operations involved in the manufacture of the OraSure HIV-1 Western Blot Kit are conducted at Epitope, Inc. in Beaverton, Oregon with two exceptions. The propagation and inactivation of viral lysate and irradiation of powdered milk are conducted by outside vendors.

Inactivated and denatured proteins of the HIV-1 virus are fractionated by SDS-polyacrylamide gel electrophoresis. The resolved protein bands are electrophoretically transferred to nitrocellulose sheets. These preblotted nitrocellulose sheets are cut into strips. Finished strips must meet in-house specifications for performance and sensitivity by testing against an in-house quality control panel prior to release.

Reactive and non-reactive control sera have been tested for the presence of HBsAg and antibody to HCV. Reactive controls have been heat-inactivated to render material noninfectious for HIV-1.

The controls are assayed for HIV-1 antibody reactivity and must exhibit a similar pattern to the internal quality control reference material. The High Positive Control must show reactivity with the major virus-specific bands at positions of 160, 120, 65, 51, 41, 31, 24, and 18 kd. The Low Positive Control must show reactivity with bands at positions 160, 41 and 24 kd. Other reactivity may or may not be present.

IV. Warnings and Limitations in Use

- **This test kit may not be used to assay blood specimens. This test kit may only be used to assay OraSure HIV-1 oral fluid specimens obtained using the OraSure HIV-1 Oral Specimen Collection Device.**
- **The assay must be performed in strict accordance with these instructions to obtain accurate, reproducible results.**
- **Although a Positive result may indicate infection with the HIV-1 virus, a diagnosis of Acquired Immunodeficiency Syndrome (AIDS) can be made only if an individual meets the case definition of AIDS established by the Centers for Disease Control. A repeat test on an independent sample should be considered to control for sample mix-up or operator error, and to verify a positive test result.**
- **Individuals may present incomplete banding patterns due to the natural history of AIDS or other immunodeficiency states, e.g.:**
  - **AIDS patients may lose antibody reactions to p24 and p31;**
  - **Infants born to HIV-1 infected mothers, but who are uninfected, may display incomplete patterns as passively acquired maternal antibodies begin to**

disappear;

- **Individuals who have recently seroconverted may display incomplete band patterns;**
- **Infected patients with malignancies and individuals receiving immunosuppressive drugs may fail to develop a Positive result;**
- **Individuals infected with HTLV- I/II or HIV-2, may exhibit cross-reactivity;**
- **Individuals may develop incomplete patterns that reflect the composition of experimental HIV sub-unit vaccines they may have received.**

- **Since reactivity of any degree with any of the proteins present on the strip results in an indeterminate result, all samples interpreted as Indeterminate should be repeated using the original specimen. In addition, individuals with indeterminate results should be followed for up to six months.**
- **Do not use this kit as the sole basis of diagnosis of HIV-1 infection.**
- **A Negative result does not exclude the possibility of HIV-1 infection.**
- **The OraSure HIV-1 Western Blot Kit is a biological product which, although highly consistent, does display variation from lot to lot. Examples of these variations include bands which have a slightly wavy or slanted appearance, small artifacts within the banding area, and a light smearing pattern across a set of strips. These are considered normal assay variations which infrequently affect assay interpretation. However, if they do interfere with the assay interpretation, call the assay invalid and repeat.**

V. Alternative Practices and Procedures

EIA and Western blot testing can be performed on serum and plasma specimens.

VI. Marketing History

The OraSure HIV-1 Western Blot Kit has not been commercially marketed to date in the U.S. or any foreign country.

VII. Potential Adverse Effects of the Device on Health

Use of the OraSure HIV-1 Western Blot Kit has not produced any known adverse effects on health.

VIII. Summary of Studies

A. Non-clinical Studies

1. Analytical Sensitivity

Three studies were performed to characterize the analytical sensitivity of the OraSure HIV-1 Western Blot Kit.

Study I: Titration of Matching OraSure and Serum Specimens

This study involved the titration of 15 randomly selected matching OraSure and serum repository specimens that had been obtained from HIV-positive individuals. Titrated serum specimens were tested with the licensed serum HIV-1 Western Blot Kit and matching titrated OraSure specimens were tested in parallel with the OraSure HIV-1 Western Blot Kit. The assay endpoint in this study was the last dilution at which a positive Western blot result was observed for each specimen.

Study II: Titration of OraSure Seroconversion Specimens

In support of the original OraSure device PMA (#BP910001), matching OraSure and plasma specimens were acquired from an individual undergoing HIV-1 seroconversion during May, 1991. Repository specimens from this seroconversion study were used to assess the analytical sensitivity of the OraSure HIV-1 Western Blot Kit.

Study III: OraSure Control Matrix Spiked with HIV-1 Positive Serum from a Seroconverter

This study involved the use of members of a commercially available HIV-1 serum conversion panel which contained antibodies directed primarily against the p24 viral protein.

2. Failure Mode Analysis

The OraSure HIV-1 Western Blot Kit was subjected to a variety of stresses in an effort to determine how resistant the assay is to failure. The two major conditions evaluated were operator-related error and component failure.

Each condition was monitored by the testing of six OraSure HIV-1 Western Blot Kit strips with a panel consisting of three OraSure HIV-1 Western Blot Kit controls (high positive, low positive, and negative) and three OraSure specimens. Two of the three OraSure specimens were collected from HIV-1 positive individuals and the remaining specimen was collected from an HIV-1 negative individual.

3. Reproducibility

The reproducibility of the OraSure HIV-1 Western Blot Kit was evaluated at three separate test laboratories. The study included testing a three-member panel of pooled OraSure specimens with the OraSure HIV-1 Western Blot Kit. The OraSure

reproducibility panel consisted of an HIV-1 positive specimen, an HIV-1 negative specimen, and an HIV-1 Western blot indeterminate specimen. The panel members were tested on three separate days using three separate OraSure HIV-1 Western Blot Kit production lots on each of three days, with a total of 27 test results generated for each panel member.

4. Stability

A number of studies have been conducted to evaluate the stability of the components of the OraSure HIV-1 Western Blot Kit. Real-time studies of three separate lots of each component of the OraSure HIV-1 Western Blot Kit were performed (both bulk and finished goods). Components for stability testing were held at 4°C and then tested in the OraSure HIV-1 Western Blot Kit. Test points for all bulk components included baseline (T = 0), 24 hours, 48 hours, 7 days, 14 days, 21 days, 28 days, 42 days, 2 months, 3 months, Monthly test intervals continued until the component under evaluation reached study completion. Following baseline testing (T = 0), finished goods components were tested at monthly intervals.

B. Preclinical Studies

Sensitivity and specificity studies were performed on matched OraSure and serum specimens from a total of 204 HIV-1 negative subjects and 226 HIV-1 positive subjects.

C. Clinical Studies

The performance of the OraSure HIV-1 Western Blot Kit was evaluated by comparing OraSure results with those obtained from matched serum specimens tested by a licensed HIV-1 Western blot. These specimens were collected prospectively in a clinical study of low risk (n = 2,382), high risk (n = 698), and AIDS (n = 242) populations. In addition, non-specificity specimens (n = 248) were obtained from subjects with non-HIV-1 related medical conditions that might result in antibodies cross-reactive with HIV-1 proteins. All the high risk and AIDS subjects, and 495 of the low risk subjects were tested by Western blot, irrespective of their EIA results. EIA testing of an additional 1,887 "screen only" low risk subjects was carried out using the Organon Teknika Oral Fluid Vironostika HIV-1 Microelisa System in an effort to find EIA repeatedly reactive samples (from uninfected individuals) with which to challenge the OraSure Western blot. Testing of the 1,887 "screen only" subjects identified 14 OraSure specimens as repeatedly reactive. These 14 OraSure specimens and their matching sera were also advanced to Western blot testing. Thus, a total of 1,697 matched OraSure and serum specimens were tested by Western blot at five testing laboratories throughout the United States.

Low risk subjects were persons with no known risk factors; primarily normal blood

donors. Of the 698 high risk specimens, 363 were from homosexuals, 116 from injection drug users (IDUs), 83 from persons with multiple heterosexual contacts, and 44 from hemophiliacs. The remaining 92 high risk subjects included bisexuals, prostitutes, and individuals with other acknowledged risk factors. Specimens from 242 persons with clinically diagnosed AIDS were also tested.

The frequency of virus-specific bands and interpretation by risk group using the OraSure HIV-1 Western Blot Kit are presented in Table 1.

Table 1: Frequency of Virus-Specific Bands ("Present" or "Indeterminate") and Interpretation of Specimens Tested by the OraSure HIV-1 Western Blot Kit

Low Risk[a]	OraSure HIV-1 WB Result		Band Specificities (# and % of samples)[g]									Non-Viral
			gp160	gp120	p65	p55	p51	gp41	p31	p24	p18	
EIA neg. n=495	POS	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	IND	100[b] (20.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (1.0)	0 (0.0)	13 (2.6)	2 (0.4)	87 (17.6)
EIA RR[h] n=14	POS	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	IND	3[c] (21.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (7.1)	0 (0.0)	2 (14.3)

High Risk[d]	OraSure HIV-1 WB Result		Band Specificities (# and % of samples)[g]									Non-Viral
			gp160	gp120	p65	p55	p51	gp41	p31	p24	p18	
EIA neg. n=264	POS	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	IND	45[e] (17.0)	4 (1.5)	0 (0.0)	6 (2.3)	0 (0.0)	5 (1.9)	0 (0.0)	0 (0.0)	8 (3.0)	0 (0.0)	33 (12.5)
EIA RR[h] n=434	POS	429 (98.8)	429 (98.8)	427 (98.4)	417 (96.1)	160 (36.9)	412 (94.9)	427 (98.4)	394 (90.8)	410 (94.5)	238 (54.8)	1 (0.2)
	IND	3 (0.7)	3 (0.7)	2 (0.5)	2 (0.5)	0 (0.0)	2 (0.5)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

AIDS[f]	OraSure HIV-1 WB Result		Band Specificities (# and % of samples)[g]									Non-Viral
			gp160	gp120	p65	p55	p51	gp41	p31	p24	p18	
EIA neg.	POS	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

n=1	IND	1 (100.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)
EIA RR[h]	POS	236 (97.9)	236 (97.9)	236 (97.9)	211 (87.6)	35 (14.5)	207 (85.9)	236 (97.9)	190 (78.8)	189 (78.4)	87 (36.1)	0 (0.0)
n=241	IND	5 (2.1)	5 (2.1)	4 (1.7)	1 (0.4)	0 (0.0)	1 (0.4)	4 (1.7)	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)

a. Persons with no known risk factors; primarily normal blood donors.
b. Eighty of 100 results Indeterminate due to non-viral bands only.
c. Two of 3 results Indeterminate due to non-viral bands only.
d. Homosexuals, IDUs, and other accepted risk designations.
e. Thrity-two of 45 results Indeterminate due to non-viral bands only.
f. CDC Classification; MMWR 1982; 31: 507-508.
g. Band patterns for negative samples do not appear in this table. By definition, negative samples show no reactivity.
h. RR indicates repeatedly reactive OraSure EIA results.

1. Sensitivity Studies

The performance of the OraSure Western blot in seropositive subjects was evaluated by comparing results to those obtained by testing matched serum samples collected from individuals at high risk for HIV infection and from clinically diagnosed AIDS patients. A comparison of OraSure and serum results is presented in Table 2.

Table 2: OraSure and Serum Western Blot Results for Confirmed Positive High Risk and AIDS Populations

		OraSure Specimen Results				Serum Results		
Risk Category	Confirmed Positives	EIA	Western Blot			Western Blot		
		RR	P	I	N	P	I	N
AIDS	242	241[a]	236	6[a,b]	0	241	1	0
High Risk	431	431	429	2[c]	0	431	0	0
Total	673	672	665	8	0	672	1	0

a. One OraSure sample was EIA non-reactive Western blot indeterminate (gp160+, p24+/-); the matching serum sample was EIA repeatedly reactive and Western blot positive (gp160+, gp120+, p65+, p51+, p24+).
b. One of the six Western blot indeterminate OraSure samples was repeatedly reactive on EIA and concordant on Western blot with an indeterminate result for the matching serum specimen. The remaining five OraSure specimens were discordant (indeterminate) with the matching serum specimens (positive) due to the required cardinal bands being visible but of insufficient intensity to be scored as present.
c. One OraSure sample was discordant due to the intensity of bands on the OraSure Western blot (gp160+, gp120+/-, p65+/-, p51+/-, gp41+/-). The banding pattern of the second indeterminate OraSure sample was gp160+, gp120+/-. The matching serum specimens' banding patterns were gp160+, gp120+, p65+, p51+/-, gp41+, p24+/-, p18+/- and gp160+, gp120+, p65+/-, gp41+, p24+/-, p18+/-, respectively.

RR = Repeatedly Reactive; P = Positive; I = Indeterminate; N = Negative.

In this study, the sensitivity of the OraSure Western blot testing of oral specimens from the 242 confirmed positive AIDS subjects was 97.5% (236/242) with 2.5% (6/242) indeterminate, and from the 431 confirmed positive high risk subjects was 99.5% (429/431) with 0.5% (2/431) indeterminate, with no OraSure Western blot false negatives in either group. All OraSure indeterminate blots showed the gp160 band as present and at least one additional cardinal band (gp120, gp41, p24) as visible, but of insufficient intensity to be called present. One of the OraSure indeterminate blots corresponded to the Western blot indeterminate serum specimen.

2. Specificity Studies

The performance of the OraSure Western blot in an uninfected population was evaluated by testing specimens from 495 EIA negative subjects (using oral fluid) at low risk for HIV-1 infection, 14 EIA repeatedly reactive specimens found by screening 1,887 persons at low risk for HIV-1 infection, 248 subjects with non-HIV related medical conditions (non-specificity subjects), and 267 specimens from high risk seronegative subjects. Thus, a total of 1,024 OraSure HIV-1 Western blots and serum Western blots were performed on these individuals. The results of this testing are presented in Table 3.

Table 3: Comparative Study of Western Blot Results in Low Risk, Non-Specificity, and High Risk HIV-1 Negative Populations

EIA Result for OraSure Specimens	OraSure HIV-1 Western Blot Interpretation	Licensed Serum HIV-1 Western Blot Interpretation			
		Positive	Ind.	Negative	Total
EIA Negative (n=1,007)	Positive	0	0	0	0
	Indeterminate	0	96	111	207
	Negative	0	295	505	800
EIA RR (n=17)	Positive	0	0	0	0
	Indeterminate	0	3	1	4
	Negative	0	7	6	13
	Total	0	401	623	1,024

Seventeen OraSure specimens (14 low risk and three high risk) were EIA repeatedly reactive. Thirteen of the 17 EIA false positive specimens were correctly identified as negative by the OraSure HIV-1 Western blot. Thus, 2,893 out of

2,897 subjects (99.9%) were correctly identified as HIV-1 antibody negative by a combination of EIA and Western blot testing of OraSure samples. The four remaining specimens were indeterminate by OraSure HIV-1 Western blot (two of the four due to non-viral bands only). The indeterminate rate for uninfected persons who are EIA repeatedly reactive by OraSure was 23.5% (4/17) as compared to 58.8% (10/17) for serum.

Western blot was also performed on serum and OraSure specimens from 1,007 EIA negative subjects (using oral fluid). This testing identified 20.6% of OraSure specimens and 39.2% of sera as indeterminate. The overall concordance between the two types of specimens was 59.6%. Differences were largely due to non-viral bands that were present for one type of sample but not the other for individual subjects.

3. Reactivity in Other Disease Conditions

Matching OraSure and serum specimens were obtained at three sites from 248 subjects who were enrolled in the clinical trial because they had non-HIV-1 medical conditions that might result in antibodies cross-reactive with HIV-1 proteins or other potentially interfering factors. Specimens studied included 89 from multiparous women, 69 from subjects with non-HIV viral infections, 50 receiving anticoagulation therapy, 26 with autoimmune diseases other than AIDS, 11 with oral pathology, and 3 with polyclonal or monoclonal gammopathy. Although bands were present at viral band locations for four samples (1.6%), none of the strips could be interpreted as positive. Results are presented in Table 4.

Table 4: Results of OraSure Western Blot Testing on Samples from Subjects with Non-HIV Disease Processes or Other Potentially Interfering Factors

OraSure HIV-1 WB Result	Band Specificities (# and % of samples)									Non-Viral
	gp160	gp120	p65	p55	p51	gp41	p31	p24	p18	
NEG 186 (75.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
IND 62[a] (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.2)	0 (0.0)	2 (3.2)	1 (1.6)	58 (93.5)
Total 248 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	0 (0.0)	2 (0.8)	1 (0.4)	58 (23.4)

a. 58 of 62 results Indeterminate due to non-viral bands only.

Testing of specimens from this population revealed that the number of OraSure indeterminates (62; 25.0%) was substantially less than the number of serum indeterminates (121; 48.8%). The number of serum indeterminates due to the presence of viral bands (27; 10.9%) was substantially greater than the number of OraSure indeterminates due to the presence of viral bands (4; 1.6%).

IX. Conclusions Drawn from Studies

A. Conclusions from Non-clinical Studies

Results of the analytical sensitivity studies of the OraSure HIV-1 Western Blot Kit revealed that it is more sensitive than the Oral Fluid Vironostika HIV-1 EIA in detecting HIV-1 antibodies. However, in the titration study of matching OraSure and serum specimens, the OraSure HIV-1 Western Blot Kit was shown to be less sensitive than the licensed serum Western Blot Kit.

In the failure mode study, the exact point of assay failure was not reached for all the conditions evaluated during the study. However, the last point at which the assay did not fail indicated that the assay is rugged and resistant to failure.

Reproducibility study results demonstrated that for positive specimens, negative specimens, and indeterminate specimens with known banding patterns, reproducibility is high.

Based on the results of the stability study, the expiration dating claim on the entire OraSure HIV-1 Western Blot Kit is 18 months (based on the shortest dated component).

B. Conclusions from Pre-clinical Studies

In preclinical sensitivity testing, the OraSure HIV-1 Western Blot Kit result was positive in 224 of the 226 specimens found to be positive by serum HIV-1 Western blot testing. The remaining two OraSure specimens were indeterminate based on the presence of viral bands. No OraSure false negatives were identified.

In preclinical specificity testing, the total number of indeterminates was slightly less with the OraSure HIV-1 Western Blot (27.5%) than with the serum HIV-1 Western blot (29.9%). The number of indeterminates due to the presence of viral bands was also less for the OraSure HIV-1 Western Blot (5.4%) than for the serum HIV-1 Western blot (9.8%). No OraSure HIV-1 Western Blot false positives were detected.

C. Conclusions from Clinical Study

In this clinical trial using the recommended OraSure algorithm, 3,558/3,570 subjects received the correct HIV-1 antibody results from a single OraSure sample the first time it was tested. In 11 of the remaining subjects, the Western blot was indeterminate: for these 11, the algorithm would lead to appropriate follow-up testing. Thus, in 3,569/3,570 (99.97%) of subjects, either the correct result was reached or appropriate follow-up testing would be triggered. It is concluded that OraSure testing is a highly accurate alternative to serum testing.

X. Benefits Analysis

Testing for HIV-1 antibodies using the OraSure HIV-1 Oral Specimen Collection Device offers the benefits of a non-invasive method of specimen collection: greater safety in the collection and handling of specimens, increased patient compliance, and an alternative to phebotomy in subjects with difficult venous access. It also has the advantage of making it possible to expand HIV-1 antibody testing and counseling through outreach programs in which specimen collection is taken into settings where phebotomy is difficult or impossible. These potential benefits will be fully realized when tests are available that permit the completion of the standard HIV-1 testing algorithm: screening and confirmation on a single oral fluid sample. Presently, FDA has approved the OraSure HIV-1 Oral Specimen Collection Device (Epitope, Inc.) and the Oral Fluid Vironostika HIV-1 Microelisa System (Organon Teknika Corp.). However, following a repeatedly reactive OraSure screening result the subject must be asked to provide a blood sample for confirmation of the OraSure screening result by an approved blood confirmatory test. This requirement has limited the usefulness of this innovative technology by introducing unacceptable delays in producing a confirmed HIV-1 antibody test result. Availability of the OraSure HIV-1 Western blot will allow the timely confirmation of screening results on a single OraSure sample.

XI. Panel Recommendations

An Advisory Committee Panel was not convened to review the OraSure HIV-1 Western Blot Kit.

XII. FDA Decision

Satisfactory information was submitted to FDA in the following documents: PMA submitted 6/8/95 and amendments submitted 8/24/95, 11/6/95 and 1/10/96. Epitope was issued a letter declaring the device to be "Approvable" on December 22, 1995.

An inspection of the Epitope manufacturing facilities was conducted from January 22 - February 5, 1996. Facilities and procedures were found to comply with Good Manufacturing Practices. CBER issued an approval order for the above PMA on May ___, 1996.

XIII Approval Specifications

See attached labeling (Attachment A) and Conditions of Approval (Attachment B).

5/31/96
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