AUG 1 5 1997

SUMMARY BASIS OF APPROVAL

Reference No.:	95-0120/21 (PLA) 95-0130 (ELA)	Proper Name:	Human T-Lymphotropic Virus Types I and II
Applicant:	Abbott Laboratories 100 Abbott Park Road Abbott Park, IL 60064	Product Trade Name:	Abbott HTLV-I/HTLV-II EIA

I. Indications for Use

ABBOTT HTLV-I/HTLV-II EIA is an *in vitro* enzyme immunoassay for the qualitative detection of antibodies to Human T-Lymphotropic Virus Type I and/or Type II (HTLV-I/HTLV-II) in human serum or plasma. The ABBOTT HTLV-I/HTLV-II EIA is intended to be used as a screen for donated blood to prevent transmission of HTLV-I and HTLV-II to recipients of cellular blood components and as an aid in the clinical diagnosis of HTLV-I and HTLV-II infection and related diseases.

II. Brief Description of Test

The ABBOTT HTLV-I/HTLV-II assay utilizes a bead as a solid phase, coated with detergent-solubilized and sonicated HTLV-I and HTLV-II proteins to bind antibodies to HTLV-I and/or HTLV-II from human serum or plasma. Goat antibodies directed against human immunoglobulins, conjugated with horseradish peroxidase, are then incubated with the bead. Finally, the beads are incubated with o-phenylenediamine (OPD) substrate solution containing hydrogen peroxide. A yellow-orange color develops if antibodies present in the sample bind to the bead.

The ABBOTT HTLV-I/HTLV-II EIA kit consists of the following components:

List No.7A92 ABBOTT HTLV-I/HTLV-II EIA (100/1000/5000 tests)

1) 1 Vial (100 beads each) / 2 Vials (500 beads each) / 10 Vials (500 beads each) Human T-Lymphotropic Virus Type I (Inactivated) and Human T-Lymphotropic Virus Type II (Inactivated) Coated Beads.

2) 3 Vials (1 mL each)/3 Vials (5 mL each) / 15 Vials (5 mL each) Conjugate Concentrate. Goat Antibody to Human IgG: Peroxidase (Horseradish). Minimum concentrations: 1.6 µg/mL in TRIS buffer with 10% Animal Serum (Calf) and Red Dye No. 33. Preservatives: ProClin™300 (Isothiazolone) and 0.01% Gentamicin.

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3) 3 Vials (19 mL each) / 3 Vials (95 mL each) / 15 Vials (95 mL each) Conjugate Diluent containing 20% Animal Sera (Goat, Calf) in TRIS buffer. Preservatives: ProClin™300 (Isothiazolone) and 0.01% Gentamicin.

4) 1 Vial (2 mL) / 2 Vials (2 mL each) / 10 Vials (2 mL each) HTLV-I Positive Control. Inactivated Human Plasma, reactive for antibodies to HTLV-I, nonreactive by FDA licensed tests for antibodies to HIV-1/HIV-2 and HCV, and nonreactive for HBsAg, with bromophenol blue dye added. Minimum titer: 1:5. Preservative: 0.1% Sodium Azide. HTLV-I Positive Control may be cross-reactive with antibody to HTLV-II.

5) 1 Vial (2 mL)/2 Vials (2 mL each)/10 Vials (2 mL each) Negative Control. Human Plasma nonreactive by FDA licensed tests for antibodies to HTLV-I, HIV-1/HIV-2 and HCV, and nonreactive for HBsAg. Preservative: 0.1% Sodium Azide.

6) 1 Vial (100 mL)/4 Vials (100 mL each)/20 Vials (100 mL each) Specimen Diluent containing 30% Animal Sera (Goat, Calf) in TRIS buffer. Preservative: 0.1% Sodium Azide.

7) 1 Vial (2 mL)/2 Vials (2 mL each)/10 Vials (2 mL each) HTLV-II Positive Control. Inactivated Human Plasma reactive for antibodies to HTLV-II, nonreactive by FDA licensed tests for antibodies to HIV-1/HIV-2 and HCV, and nonreactive for HBsAg. Minimum Titer: 1:5. Preservative: 0.1% Sodium Azide. HTLV-II Positive Control may be cross-reactive with antibody to HTLV-I.

- There is no reagent 8.

9) 1 Bottle (10 Tablets)/2 Bottles (40 Tablets each)/ 10 Bottles (40 tablets each) OPD (o-phenylene-diamine • 2 HCl) Tablets. OPD/Tablet: 12.8 mg

10) 1 Bottle (55 mL)/2 Bottles (220 mL each)/10 Bottles (220 mL each) Diluent for OPD (o-phenylenediamine • 2 HCl). Citrate Phosphate Buffer containing 0.02% Hydrogen Peroxide.

Other Reagents:

11) 1 *N* Sulfuric Acid, No. 7212. Use of acid other than that supplied by ABBOTT may result in instability of the developed color.

III. Manufacturing and Controls

A. Manufacturing and Controls

ABBOTT HTLV-I/HTLV-II EIA is prepared under U.S. License Number 43 by Abbott Laboratories. Two cell lines are used to produce the HTLV-I and HTLV-II antigens coated on the bead. HTLV-I is obtained from the chronically infected human T-lymphocyte cell line HUT 102.B2 and HTLV-II from the chronically infected human B-lymphocyte cell line WIL-NRA. The cell lines are expanded in medium and maintained in tissue culture. Virus is recovered and purified by sucrose gradient centrifugation, and inactivated viral lysate is produced through detergent solubilization and sonication of the virus particles. These inactivated viral lysates are then coated on polystyrene beads. The HTLV-I Positive Control, HTLV-II Positive Control and Negative Control are prepared from human plasma, which is recalcified and nonreactive for HBsAg, anti-HIV-1/anti-HIV-2 and anti-HCV. The HTLV-I and HTLV-II Positive Controls are inactivated by heating at 60°C for one hour.

Raw materials intended for use in the product are subjected to appropriate quality control evaluations before they are accepted for use in manufacturing. Acceptance criteria and performance specifications have been established for all test kit components. Components are assembled into test kits and each lot of test kits is subjected to a final performance test.

Each lot of ABBOTT HTLV-I/HTLV-II EIA is tested with in-house panels of samples with varying levels of anti-HTLV-I and/or anti-HTLV-II reactivities, as well as the CBER HTLV-I and HTLV-II Reference Panels, and must meet the performance requirements of both panels.

B. Stability Studies

The stability of ABBOTT HTLV-I/HTLV-II EIA has been established based upon testing at the recommended storage conditions of 2 to 8°C. Four different lots of each component were manufactured, tested, assembled into master lots and evaluated during storage. The studies indicate no compromise in product performance to date and support a 15 month dating period for the test kit.

C. Methods of Validation

Production of the test kit components is monitored by in-process testing. Product potency is assured through evaluation of product appearance, sterility or bioburden tests and performance. Product consistency is assured through lot uniformity testing of components. Product performance is assessed through laboratory evaluations of each test kit against in-house panels and the CBER HTLV Reference Panel. Each lot of product and protocols summarizing pertinent product testing are submitted for evaluation and approval by FDA prior to release for distribution.

D. Labeling

The product labeling, including immediate container, package labels and package insert (directions for use), are in compliance with 21 CFR 610.60, 610.61, 610.62 and 809.10. The product trade name, ABBOTT HTLV-I/HTLV-II EIA, is not known to conflict with any other biologic or device trade name.

E. Establishment Inspection

A prelicensing inspection of the areas where product is manufactured, tested, stored and shipped was conducted from March 11 to March 14, 1997. Facilities and procedures were found to comply with current good manufacturing practices.

F. Environmental Impact Analysis Report (EIAR)

A detailed EIAR was filed by the manufacturer. This product has no significant environmental impact.

IV. Biological Principles of the Procedure

The ABBOTT HTLV-I/HTLV-II EIA is a solid phase immunoassay used to detect antibodies to HTLV-I and HTLV-II in human serum or plasma.

• Sample (specimen or control) is diluted in specimen diluent and incubated with a polystyrene bead coated with detergent solubilized HTLV-I and HTLV-II proteins (inactivated).

• Specific antibodies present in the sample bind to the HTLV-I and HTLV-II antigens on the bead.

• Unbound materials are removed by washing the beads.

• Goat antibody directed against human IgG that has been conjugated with horseradish peroxidase (anti-human IgG: HRPO) is then incubated with the beads and binds to the human IgG on the solid phase.

• Unbound conjugate is removed by washing the beads.

• The beads are then incubated with o-phenylenediamine (OPD) substrate solution containing hydrogen peroxide. The reaction of OPD substrate solution with HRPO yields a yellow-orange color. The intensity of the color formed is proportional to the amount of HTLV-I and/or HTLV-II antibody present in the sample.

• The enzyme reaction is stopped by the addition of 1 *N* Sulfuric Acid and the intensity of the color developed is read using a spectrophotometer.

Specimens with absorbance values less than the assay Cutoff Value are considered negative for antibodies to HTLV-I and/or HTLV-II by the criteria of the ABBOTT HTLV-I/HTLV-II EIA. Specimens with absorbance values greater than or equal to the assay Cutoff Value are considered initially reactive by the criteria of the ABBOTT HTLV-I/HTLV-II EIA. Initially reactive specimens are to be retested in duplicate using the original sample of serum or plasma. If one or both duplicate retest samples are reactive, the specimen is considered repeatedly reactive for antibodies to HTLV-I and/or HTLV-II by the criteria of the ABBOTT HTLV-I/HTLV-II EIA. If both of the duplicate retest samples are non-reactive, the specimen is considered negative for antibodies to HTLV-I and/or HTLV-II by the criteria of the ABBOTT HTLV-I/HTLV-II EIA.

V. *Performance Characteristics*

A. *Summary of Studies Conducted at Abbott Laboratories*

1. Studies were performed to support the use of the ABBOTT HTLV-I/HTLV-II EIA in the testing of samples collected with and without various anti-coagulants. Specimens from ten donors were collected in various tube types, divided into aliquots, and left unspiked (control) or spiked with either anti-HTLV-I or anti-HTLV-II positive plasma. The following specimen collection types were evaluated for use in the assay:

- Serum (no additive)
- Serum from Serum Separator Tubes
- Plasma from anti-coagulated whole blood containing,
    a. Acid/citrate/dextrose (ACD)
    b. Sodium citrate
    c. Citrate/phosphate/dextrose/adenine (CPDA-1)
    d. Citrate/phosphate/dextrose (CPD)
    e. Citrate/phosphate/double dextrose (CP2D)
    f. Sodium EDTA
    g. Potassium EDTA
    h. Heparin
    i. Potassium oxalate

All negative donor specimen results remained negative and all anti-HTLV-I and all anti-HTLV-II spiked samples remained positive. These data demonstrated that all of the specimen collection types listed above were suitable for use in the ABBOTT HTLV-I/HTLV-II EIA.

2. Sample stability studies were performed to evaluate storage of various specimen collection types for up to 14 days at the intended storage condition of 2 to 8• C. Specimens from ten donors were collected in various tube types, divided into aliquots, and left unspiked (control) or spiked with either anti-HTLV-I or anti-HTLV-II positive plasma. The following specimen collection types were evaluated:

- Serum (no additive)
- Serum from Serum Separator Tubes
- Plasma from anti-coagulated whole blood containing,
    a. Acid/citrate/dextrose (ACD)
    b. Sodium citrate
    c. Citrate/phosphate/dextrose/adenine (CPDA-1)
    d. Citrate/phosphate/dextrose (CPD)
    e. Citrate/phosphate/double dextrose (CP2D)
    f. Sodium EDTA
    g. Potassium EDTA
    h. Heparin
    i. Potassium oxalate

All negative donor specimen results remained negative and all anti-HTLV-I and all anti-HTLV-II-spiked samples remained positive throughout the 14 day testing

period. These data support the stability of negative and positive samples stored at 2 to 8°C for up to 14 days using any of the listed specimen collection types.

3. Studies were performed to provide data to assess the effects of various shipping conditions and of multiple freeze-thaw cycles on negative and positive (anti-HTLV-I and anti-HTLV-II spiked) plasma and serum samples for use in the ABBOTT HTLV-I/HTLV-II EIA. Specimens from ten donors were collected into potassium EDTA and serum tubes, divided into aliquots and left unspiked (control) or spiked with anti-HTLV-I or anti-HTLV-II positive plasma. Samples types were tested over seven days at -10°C and 37°C, and over 14 days at 2 to 8°C as well as ambient temperature. Samples were also tested after three freeze-thaw cycles. The data showed that serum and plasma specimens may be shipped at -10°C, 2 to 8°C, ambient and 37°C. The data also showed that three freeze-thaw cycles did not effect the performance of the ABBOTT HTLV-I/HTLV-II EIA.

4. Studies were performed to investigate the effect of heat-inactivation (56°C for 30 minutes) on negative and positive samples for use in the ABBOTT HTLV-I/HTLV-II EIA. Specimens from 15 donors were collected into potassium EDTA tubes and the plasma removed from each tube was divided into three aliquots: unspiked (control), anti-HTLV-I positive (spiked) and anti-HTLV-II positive (spiked) samples. The effect of heating on the three sample types was an increase in the sample/cutoff values, therefore it is recommended that samples not be heat-inactivated prior to evaluation with the ABBOTT HTLV-I/HTLV-II EIA.

5. Studies were performed to provide data to evaluate the effects of various potentially interfering substances found in specimens for use in the ABBOTT HTLV-I/HTLV-II EIA. Substances included in this study were bilirubin, hemoglobin, triglycerides and total protein. Specimens from ten donors were collected into serum separator tubes and spiked with the appropriate level of the potentially interfering substances. Each of these samples was then divided into three aliquots: unspiked (control), anti-HTLV-I positive (spiked) and anti-HTLV-II positive (spiked) samples. The study revealed that bilirubin (up to 20 mg/dL), hemoglobin (up to 2000 mg/dL), triglycerides (up to 2190 mg/dL) and total protein (up to 14 g/dL) in a sample do not interfere with the ABBOTT HTLV-I/HTLV-II EIA.

6. A study was performed to evaluate samples with a history of false positive reactivity on multiple tests for use in the ABBOTT HTLV-I/HTLV-II EIA. These "multi-reactive" samples and some vaccine recipient samples have IgM antibodies that bind nonspecifically to the solid support. This study demonstrated that the false positive reactivity for these categories of specimens was less frequent using

the anti-human IgG (gamma specific) conjugate in the ABBOTT HTLV-I/HTLV-II EIA compared to an anti-human IgM (mu specific) conjugate, such as that used in the ABBOTT HTLV-I 2.0 EIA. The ABBOTT HTLV-I/HTLV-II EIA will produce a lower false positive rate than the ABBOTT HTLV-I 2.0 EIA when these types of samples are encountered.

B. Summary of Clinical Data

1. Reproducibility

Assay reproducibility of the ABBOTT HTLV-I/HTLV-II EIA was determined by testing a 28 member panel consisting of four replicates each of three diluted HTLV-I antibody containing specimens, three diluted HTLV-II antibody containing specimens and one specimen nonreactive for antibody to HTLV-I or HTLV-II. The panel was tested over a minimum of five days for each of three master lots at a total of eight sites. The inter-assay and intra-assay reproducibility of testing these specimens are shown in Table I.

2. Specificity

Specificity of the ABBOTT HTLV-I/HTLV-II EIA was estimated from screening tests of random U.S. blood donors (plasma, serum and plasmapheresis specimens). A total of 15,215 serum and plasma specimens from volunteer blood donors and plasmapheresis donors were collected from five geographically distinct U.S. blood centers (Table II). Three sites tested a total of 5,909 serum specimens and had an overall initial reactive rate of 0.32% (19/5,909) and repeatedly reactive rate of 0.30% (18/5,909) by the ABBOTT HTLV-I/HTLV-II EIA. Of the 18 repeatedly reactive serum specimens, four (22.22%) tested positive, 11 were indeterminate and three were negative by investigational Western blot and RIPA. Two sites tested a total of 6,292 plasma specimens and had an overall initial reactive rate of 0.37% (23/6,292) and repeatedly reactive rate of 0.35% (22/6,292) by the ABBOTT HTLV-I/HTLV-II EIA. Of the 22 repeatedly reactive plasma specimens, one tested positive, 13 were indeterminate and eight were negative by investigational Western Blot and RIPA. One site tested a total of 3,014 plasmapheresis specimens and had an initial reactive rate of 0.40% (12/3,014) and repeatedly reactive rate of 0.36% (11/3,014). Of the 11 repeatedly reactive specimens, five (45.45%) tested positive, five were indeterminate and one was negative by investigational Western Blot and RIPA.

Specificity of the ABBOTT HTLV-I/HTLV-II EIA estimated from screening of

U.S. random blood donors was 99.73% (15,164/15,205) based on an assumed zero prevalence of HTLV-I and HTLV-II antibodies. Ten repeatedly reactive specimens that were positive by supplemental testing were excluded from these calculations. Therefore, of 15,205 donations presumed seronegative for HTLV-I and HTLV-II, the ABBOTT HTLV-I/HTLV-II EIA has an estimated specificity of 99.63% to 99.81% by the binomial distribution at 95% confidence.

Three sites evaluated 639 specimens from medical conditions unrelated to HTLV-I or HTLV-II. Twenty-six specimens (4.07%) were initially reactive and 26 (4.07%) were repeatedly reactive by the ABBOTT HTLV-I/HTLV-II EIA (Table II). Five of the 26 specimens tested positive by investigational Western blot or RIPA. No particular medical condition unrelated to HTLV-I or HTLV-II was significantly associated with false positive reactivity.

HTLV type differentiation of the 15 repeatedly reactive, supplemental test-positive specimens in the specificity study indicated that 7 specimens were positive for antibodies to HTLV-I and 8 specimens were positive for antibodies to HTLV-II (Table II).

3. Sensitivity

A total of 1,272 specimens were tested with the ABBOTT HTLV-I/HTLV-II EIA, including patients with HTLV-I and/or suspected HTLV-II associated disease and their contacts, populations at increased risk of HTLV-I and/or HTLV-II infection, populations from HTLV-I and/or HTLV-II endemic areas, and known HTLV-I or HTLV-II positive specimens. Of the 1,272 specimens tested, 1,233 tested positive by investigational Western blot and/or RIPA, of which 590 specimens were HTLV-I positive, 506 specimens were HTLV-II positive, and 137 specimens were untypeable HTLV-I/II positive (Table III.). The ABBOTT HTLV-I/HTLV-II EIA had an estimated sensitivity of 100% (interval of 99.76% to 100%) for 1,233 supplemental test-positive specimens by the binomial distribution at 95% confidence.

Prospective studies were performed on a total of 7,650 specimens from populations at increased risk of HTLV-I or HTLV-II infection and from populations in HTLV-I or HTLV-II endemic areas with the ABBOTT HTLV-I/HTLV-II EIA (Table IV). Of the 528 supplemental test-positive samples in these populations, 219 were HTLV-I positive, 242 were HTLV-II positive, and 67 were untypeable HTLV-I/II positive. One hundred percent of these 528 supplemental test-positive samples were repeatedly reactive on the ABBOTT HTLV-I/HTLV-II EIA.

VI. Package Insert

A copy of the package insert (directions for use) is attached.

TABLE I
ABBOTT HTLV-I/HTLV-II EIA Reproducibility

Specimen	Number of Replicates	Mean S/CO*	Intra-Assay S.D.	Intra-Assay %CV	Inter-Assay S.D.	Inter-Assay %CV
1	472	3.294	0.2544	7.7	0.3496	10.6
2	472	1.998	0.1480	7.4	0.2099	10.5
3	472	1.260	0.1085	8.6	0.1365	10.8
4	472	3.328	0.2309	6.9	0.3612	10.9
5	472	2.380	0.2274	9.6	0.2928	12.3
6	472	1.400	0.1349	9.6	0.1666	11.9
7	472	0.330	0.0372	11.3	0.0482	14.6

*Cutoff = 0.4 x PCN1 Mean

Controls	Number of Replicates	Mean O.D.	Intra-Assay S.D	Intra-Assay %CV	Inter-Assay S.D.	Inter-Assay %CV
NCN1	236	0.093	0.0115	12.3	0.0149	16.0
PCN1	236	1.135	0.0801	7.1	0.1144	10.1
PCN2	236	1.236	0.0953	7.7	0.1294	10.5

O.D. = Optical Density
NCN1 = Negative Control
PCN1 = HTLV-I Positive Control
PCN2 = HTLV-II Positive Control

TABLE II.
Reactivity In Low-Risk Populations and In Medical Conditions Unrelated to HTLV-I or HTLV-II Infection

Group/Type	Total Number of Specimens Tested	ABBOTT HTLV-I/HTLV-II EIA		Number of EIA Repeatedly Reactive Not Positive by Supplemental Testing[a] (% of Total)	Number of EIA Repeatedly Reactive Positive by Supplemental Testing[a] (% of RR)	HTLV Type Differentiation of RR Supplemental Test-Positive Specimens[b]	
		Initially Reactive (% of Total)	Repeatedly Reactive (RR) (% of Total)			HTLV-I	HTLV-II
Blood Donors							
Serum	5,909	19 (0.32)	18 (0.30)[c]	14 (0.24)	4 (22.22)	1	3
Plasma	6,292	23 (0.37)	22 (0.35)[d]	21 (0.33)	1 (4.55)	0	1
Plasmapheresis Donors	3,014	12 (0.40)	11 (0.36)[e]	6 (0.20)	5 (45.45)	3	2
Total Random Donors	15,215	54 (0.35)	51 (0.34)	41 (0.27)	10 (19.61)	4	6
Medical Conditions Unrelated to HTLV-I or HTLV-II[f]	639	26 (4.07)	26 (4.07)[g]	21 (3.28)[h]	5 (19.23)[i]	3	2

Footnotes for Table II.

[a] A positive result in these studies was defined by the presence of antibodies to two gene products (*gag*, p24 and *env*, native gp46 or gp61/67/68) using investigational Western blot and/or RIPA.

[b] HTLV-I and HTLV-II type differentiation was determined using the following investigational assays: reactivity to recombinant gp46-I or gp46-II peptides on a Western blot, HTLV-I and HTLV-II peptide EIAs, and/or PCR (using specific primers to the *tax* and *pol* regions).

[c] Four of the 18 repeatedly reactive specimens tested positive, 11 were indeterminate, and three were negative by investigational Western blot and RIPA.

[d] One of the 22 repeatedly reactive plasma specimens tested positive, 13 were indeterminate, and eight were negative by investigational Western blot and RIPA.

[e] Five of the 11 repeatedly reactive specimens tested positive, five were indeterminate and one was negative by investigational Western blot and RIPA.

[f] Included the following specimen groups: anti-CMV Positive (38); anti-EBV Positive (60); anti-HBs Positive (20); HBsAg Positive (20); anti-HCV Positive (43); anti-HIV-1 Positive (150); anti-HIV-2 Positive (10); anti-HSV Positive (20); anti-Toxoplasmosis Positive (10); Other Bacterial Infections (15); Other Diseases (9); SLE Patients (20); ANA Positive (20); Rheumatoid Arthritis (15); Hypergammaglobulinemia (10); Elevated Bilirubin (58); Elevated Hemoglobin (10); Elevated Triglycerides (15); Influenza and Tetanus Vaccine Recipients (10); Multiple Sclerosis Patients (4); Animal Handlers (5); Non-HTLV Leukemia (67); and IgM Nonspecific specimens from influenza vaccinated blood donors (10).

[g] Included specimens from the following specimen groups: anti-HCV Positive (3); anti-HIV-1 Positive (7); anti-HIV-2 Positive (1); Other Bacterial Infection (1); Elevated Bilirubin (6); Influenza Vaccine Recipients (5); Non-HTLV Leukemia (2); and IgM

Nonspecific specimen from influenza vaccinated blood donor (1).

[h] Included non-supplemental test-positive specimens from the following groups: anti-HCV positive (3); anti-HIV-1 Positive (4); anti-HIV-2 Positive (1); Elevated Bilirubin (6); Influenza Vaccine Recipients (4); Non-HTLV Leukemia (2); and IgM Nonspecific specimen from influenza vaccinated blood donor (1).

[i] Specimens that tested positive for antibodies to HTLV-I and/or HTLV-II by investigational Western blot and/or RIPA include: anti-HIV-1 Positive (3); Other Bacterial Infection (1); and Influenza Vaccine Recipient (1).

TABLE III.

Comparison of the Reactivity of the ABBOTT HTLV-I/HTLV-II EIA and the ABBOTT HTLV-I 2.0 EIA with Supplemental Test-Positive HTLV-I or HTLV-II Specimens

Group	Number of Specimens Positive by Supplemental Testing[d]	HTLV Type Differentiation of Supplemental Test-Positive Specimens[e]			Number Supplemental Test-Positive that are EIA Repeatedly Reactive (% of Supplemental Test-Positive)	
		HTLV-I	HTLV-II	Untypeable HTLV-I/II	ABBOTT HTLV-I/II EIA	ABBOTT HTLV-I 2.0 EIA
Populations with HTLV-I and/or Suspected HTLV-II Associated Disease[a]	144	141	3	0	144 (100.00)[f]	143 (99.30)
Populations at Increased Risk for HTLV-I or HTLV-II Infection and Populations from HTLV-I or HTLV-II Endemic Areas[b]	97	40	55	2	97 (100.00)[f]	96 (98.97)
Known HTLV-I or HTLV-II Positive Populations[c]	992	409	448	135	992 (100.00)	992 (100.00)
TOTAL	1,233	590	506	137	1,233 (100.00)	1,231 (99.84)

Footnotes for Table III

[a] Included the following specimen groups: ATL patients (50); TSP/HAM patients (54); Non-Hodgkin's Lymphoma (24); Southwest U.S. TSP/HAM patients infected with HTLV-II (2); and an HTLV Disease State Panel including one TSP/HAM patient infected with HTLV-II (14 members).

[b] Included the following specimen groups: Japanese Family Members of Known HTLV-I-Infected Individuals (44) and Specimens from a Southwest U.S. Endemic Area (61).

[c] Included 409 HTLV-I positive specimens, 448 HTLV-II positive specimens, and 135 untypeable HTLV-I/HTLV-II positive specimens.

[d] The number of supplemental test-positive specimens was based on supplemental test results from investigational HTLV-I/HTLV-II Western Blot and, in some cases, HTLV-I RIPA. A positive result in these studies was defined by the presence of antibodies to two gene products (*gag*, p24 and *env*, native gp46 or 61/67/68) using Western Blot and/or RIPA.

[e] HTLV-I and HTLV-II type differentiation was determined using the following investigational assays: reactivity to recombinant gp46-I or gp46-II peptides on a Western blot, HTLV-I and HTLV-II peptide EIAs, and/or PCR (using specific primers to the *tax* and *pol* regions).

[f] The additional sample detected by the ABBOTT HTLV-I/HTLV-II EIA was supplemental test-positive for anti-HTLV-I (Non-Hodgkin's Lymphoma Patient).

[g] The additional sample detected by the ABBOTT HTLV-I/HTLV-II EIA was supplemental test-positive for anti-HTLV-II (Southwestern U.S. Endemic Population).

TABLE IV.

Comparison of the Reactivity of the ABBOTT HTLV-I/HTLV-II EIA and the ABBOTT HTLV-I 2.0 EIA with Specimens from Populations at Increased Risk of HTLV-I or HTLV-II Infection and from Populations in HTLV-I or HTLV-II Endemic Areas

Group	Total Number of Specimens Tested	Number of Specimens Positive by Supplemental Testing[c]	HTLV Type Differentiation of Supplemental Test-Positive Specimens[d]			Number Supplemental Test-Positive that are EIA Repeatedly Reactive (% of Supplemental Test-Positive)	
			HTLV-I	HTLV-II	Untypeable HTLV-I/II	ABBOTT HTLV-I/II EIA	ABBOTT HTLV-I 2.0 EIA
Populations at Increased Risk for HTLV-I or HTLV-II Infection[a]	1,594	269	8	230	31	269 (100.00)[e]	269 (100.00)
Populations from HTLV-I or HTLV-II Endemic Areas[b]	6,056	259	211	12	36	259 (100.00)	259 (100.00)
TOTAL	7,650	528	219	242	67	528 (100.00)	528 (100.00)

Footnotes for Table IV.

[a] Included the following specimen groups: U.S. IV Drug Users (1,456) and specimens from Multiple Transfusion Recipients (138).

[b] Included the following specimen groups: Random Blood Donors from Central America (2,145); Amerindians from Central America (638); West Africans (20); Central Africans (38); Florida Migrant Workers predominantly from Haiti (276); Random Japanese Blood Donors (600); Random Jamaican Blood Donors (1,262); Hawaiians of Japanese Descent (215); Martinique Blood Donors (796); and Jamaican Hematology Clinic Patients (66).

[c] The number of supplemental test-positive specimens was based on HTLV-I/HTLV-II Western blot, HTLV-I RIPA, and HTLV-II RIPA investigational test results of any specimen that was repeatedly reactive or repeatedly within a 30% negative gray zone by any EIA. A positive result in these studies was defined by the presence of antibodies to two gene products (*gag*, p24 and *env*, native gp46 or 61/67/68) using Western blot and/or RIPA.

[d] HTLV-I and HTLV-II type differentiation was determined using the following investigational assays: reactivity to recombinant gp46-I or gp46-II peptides on a Western blot, HTLV-I and HTLV-II peptide EIAs, and/or PCR (using specific primers to the *tax* and *pol* regions).

LICENSING REVIEW COMMITTEE

7-18-97

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7-18-97

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