Elecsys HTLV-I/II

cobas®

REF		Σ	IVD	Rx Only	SYSTEM
09015272162	09015272502	20 x 300			**cobas pro** serology solution

English

For use in the USA only

System information

Short name	ACN (application code number)
HTLVB	10504
HTLVBE (embedded application)	11504
HTLVBR (for use with **cobas e** flow)	12504

Intended use

Elecsys HTLV-I/II is an in vitro immunoassay for the qualitative detection of antibodies to HTLV-I and HTLV-II in human serum and plasma. Elecsys HTLV-I/II is intended to screen individual human donors, including volunteer donors of whole blood and blood components. The assay is also intended to be used to screen organ, tissue and cell donors, when donor samples are obtained while the donor's heart is still beating. It is not intended for use on cord blood specimens.

The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use with **cobas pro** serology solution equipped with **cobas e** 801 analytical unit.

Summary

Human T-lymphotropic virus (HTLV) type I and type II are 2 closely related retroviruses with 70 % nucleotide sequence homology.[1] HTLV-I comprises the different subtypes A-F. The geographic areas of the highest prevalence are Japan, Africa, the Caribbean islands and South America. Additional endemic regions include the Middle East and the Melanesian islands including Papua New Guinea.[2,3] HTLV-II comprises 2 main subtypes, A and B.[4] Both are present in intravenous drug users in North America, Europe, and Asia and have been found sporadically in Africa. HTLV-II A is present in certain American Indian tribes of North, Central, and South America, including the Navajo and Pueblo in New Mexico and the Kayapo, Krahô, and Kaxuyana in Brazil.[5,6]

In addition to transmission of HTLV in intravenous drug users by needle sharing, HTLV is also transmitted from mother to child, by hetero- or homosexual intercourse and contaminated blood products.[1]

With a frequency of 15-30 %, mother-to-child transmission of HTLV has a similar frequency as that of an untreated HIV-1 infection, and occurs predominantly in the postnatal period through breastfeeding.[7]

Transmission by blood products is strictly cell-associated; the virus is not transmitted by plasma or plasma-derived products.[8] Recipients of contaminated blood seroconvert with a 40-60 % probability and an estimated seroconversion time of 51 days.[3] The majority of HTLV-I infected individuals remain lifelong asymptomatic carriers. Only 2-3 % of the HTLV-I infected individuals develop adult T-cell leukemia (ATL) and 0.25-4 % develop HTLV-I-associated myelopathy/tropical spastic paraparesis (HAM/TSP).[9] Although less than 10 % of HTLV-I carriers progress to ATL or HAM/TSP, the diseases are generally severe and progressively incapacitating. The disease type correlates with the route of infection; breastfeeding has been associated with ATL, and HAM/TSP with blood transfusion.[1] There have been some reports describing a correlation between HTLV-II infection and different diseases[10,11]; however, the evidence is not as clear as that for HTLV-I.

Test principle

Double antigen sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: 18 µL of sample, biotinylated HTLV-specific recombinant antigens (HTLV-I gp21 and HTLV-II p24) and HTLV-specific recombinant antigens (HTLV-I gp21 and HTLV-II p24) labeled with a ruthenium complex[a)] react to form a sandwich complex.
- 2nd incubation: After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin.
- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell II M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined automatically by the software by comparing the electrochemiluminescence signal obtained from the sample with the cutoff value obtained by the HTLV-I/II embedded calibration. The Elecsys HTLV-I/II result is calculated automatically based on signal to cutoff ratio (cutoff index, COI).

a) Tris(2,2'-bipyridyl)ruthenium(II)-complex ($Ru(bpy)_3^{2+}$)

Reagents - working solutions

The **cobas e** pack (M, R1, R2) is labeled as HTLVB.

M Streptavidin-coated microparticles, 1 bottle, 14.1 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 HTLV-specific recombinant antigens (E. coli)~biotin, 1 bottle, 16.7 mL:
Biotinylated HTLV-specific recombinant antigens (E. coli) approximately 0.3 mg/L; MES[b)] buffer 50 mmol/L, pH 6.2; preservative.

R2 HTLV-specific recombinant antigens (E. coli)~$Ru(bpy)_3^{2+}$, 1 bottle, 16.7 mL:
HTLV-specific recombinant antigens (E. coli) labeled with ruthenium complex approximately 0.3 mg/L; MES buffer 50 mmol/L, pH 6.2; preservative.

b) MES = 2-morpholino-ethane sulfonic acid

HTLVB Cal1 Non-reactive calibrator 1 (lyophilized), 2 vials each for 1.0 mL:
Human serum, non-reactive for anti-HTLV antibodies; preservative.

HTLVB Cal2 Reactive calibrator 2 (lyophilized), 2 vials each for 1.0 mL:
Human serum, reactive for anti-HTLV antibodies; preservative.

Precautions and warnings

For in vitro diagnostic use.

This test is not intended for use as an aid in diagnosis of HTLV infection.

Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning

H317 May cause an allergic skin reaction.

H412 Harmful to aquatic life with long lasting effects.

Prevention:

P261 Avoid breathing dust.

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P273 Avoid release to the environment.

P280 Wear protective gloves.

Response:

P333 + P313 If skin irritation or rash occurs: Get medical advice/attention.

P362 + P364 Take off contaminated clothing and wash it before reuse.

Disposal:

P501 Dispose of contents/container to an approved waste disposal plant.

Hazardous components:

- 2-methyl-2H-isothiazol-3-one hydrochloride

Product safety labeling follows EU GHS guidance.

Contact phone: 1-866-744-6397

All human material should be considered potentially infectious.

The calibrators (HTLVB Cal1 and HTLVB Cal2) have been prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV. The testing methods use assays that have been approved or cleared by the FDA or that are in compliance with the legal rules of the European Union (IVDR 2017/746/EU, IVDD 98/79/EC, Annex II, List A).

However, as no testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[12,13]

Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

Reagent handling

The reagents (M, R1, R2) in the kit are ready-for-use and are supplied in **cobas e** packs.

Calibrators

Carefully dissolve the contents of one vial by adding exactly 1.0 mL of distilled or deionized water and allow to stand closed for 15 minutes to reconstitute. Mix carefully, avoiding foam formation.

Transfer the reconstituted calibrators into the supplied empty labeled snap-cap vials.

Perform **only one** calibration procedure per vial.

All information required for correct operation is available via the **cobas** link.

Storage and stability

Store at 2-8 °C.

Do not freeze.

Store the **cobas e** pack **upright** in order to ensure complete availability of the microparticles during automatic mixing prior to use.

Stability of the **cobas e** pack:

unopened at 2-8 °C	up to the stated expiration date
on the **cobas e** 801 analytical unit	16 weeks

Stability of the calibrators:

unopened at 2-8 °C	up to the stated expiration date
reconstituted at 2-8 °C	3 days
on the **cobas e** 801 analytical unit at 20-25 °C	use only once, stable onboard for up to 5 hours

Store calibrators **upright** in order to prevent the calibrator solution from adhering to the lid of the vials.

Specimen collection and preparation

Only the specimens listed below were tested and found acceptable.

Serum and Li-heparin, K_2-EDTA, K_3-EDTA , CPD and Na-citrate plasma collected using standard sampling tubes.

Serum and Li-heparin and K_2-EDTA plasma collected in tubes containing separating gel.

Samples on-the-clot are stable for 7 days at 15-30 °C, 14 days at 2-8 °C. Do not freeze samples on-the-clot.

Samples off-the-clot are stable for 7 days at 20-25 °C, 14 days at 2-8 °C and 1 month at -20 °C (± 5 °C). Samples off-the-clot may be frozen up to 4 times.

All whole-blood samples and samples containing precipitates need to be centrifuged before performing the assay for 10 to 15 minutes at 2000 to 4000 RCF (relative centrifugal force = x g).

The sample types listed were tested with a selection of sample collection tubes or systems that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube/collection system manufacturer.

Do not use pools of samples.

Do not use heat-inactivated samples.

Do not use samples and controls stabilized with azide.

The performance of Elecsys HTLV-I/II has not been established with cadaveric samples or body fluids other than serum and plasma.

Sample stability claims were established by experimental data by the manufacturer only for the temperatures/time frames as stated in the method sheet.

Materials provided

See "Reagents – working solutions" section for reagents.

- 2 x 2 empty labeled snap-cap vials

Materials required (but not provided)

- REF 07108133162, PreciControl HTLV, for 6 x 1.0 mL
- REF 09366989190, PreciControl Release HTLV, for 6 x 1.0 mL
- REF 11776576322, CalSet vials, 2 x 56 empty snap-cap vials
- General laboratory equipment
- Distilled or deionized water
- The **cobas pro** serology solution is a combination of the **cobas pro** serology controller, **cobas pro** integrated solutions (**cobas e** 801 analytical units only) and applicable licensed or cleared donor screening assays.

Additional materials for the **cobas e** 801 analytical unit:

- REF 06908799190, ProCell II M, 2 x 2 L system solution
- REF 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- REF 07485409001, Reservoir Cup, 8 cups to supply ProCell II M and CleanCell M
- REF 06908853190, PreClean II M, 2 x 2 L wash solution
- REF 05694302001, Assay Tip/Assay Cup tray, 6 magazines x 6 magazine stacks x 105 assay tips and 105 assay cups, 3 wasteliners
- REF 07485425001, Liquid Flow Cleaning Cup, 2 adaptor cups to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning Detection Unit
- REF 07485433001, PreWash Liquid Flow Cleaning Cup, 1 adaptor cup to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning PreWash Unit
- REF 11298500160, ISE Cleaning Solution/Elecsys SysClean, 5 x 100 mL system cleaning solution

Assay

For optimum performance of the assay follow the directions given in this document for the analytical unit concerned. Refer to the appropriate user guide for analytical unit specific assay instructions.

Resuspension of the microparticles takes place automatically prior to use.

Place the cooled (stored at 2-8 °C) **cobas e** pack on the reagent manager. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the **cobas e** pack.

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Calibrators:

Place the reconstituted calibrators in the sample zone.

Read in all the information necessary for calibrating the assay.

Calibration

Calibration frequency: Calibration must be performed once per reagent lot using HTLVB Cal1, HTLVB Cal2 and fresh reagent (i.e. not more than 24 hours since the **cobas e** pack was registered on the analytical unit).

Recalibration is required as follows:

- after 12 weeks when using the same reagent lot
- after 28 days when using the same **cobas e** pack on the analytical unit
- as required: e.g. quality control findings outside the defined limits

Quality control

For quality control, use PreciControl HTLV.

Controls for the various concentration ranges must be run individually at least once every 24 hours when the test is in use, once per **cobas e** pack, and following each calibration.

PreciControl HTLV values must be within the ranges specified in the control value sheet. When the assay control values are within range, sample results are generated, and a valid release control result is required to release test results. If an assay control value is not within range, sample results are not generated for in-process or scheduled samples. For troubleshooting information, refer to User Assistance **cobas pro** serology solution or contact US Customer Technical Support.

Release control

For release control, use PreciControl Release HTLV.

Result validation is based on test result batches that are concluded by release control measurements. A release control result within defined limits is required to validate a batch of previously measured test results utilizing the **cobas pro** serology controller software. Initial reactive results will not be invalidated by a failed release control and must be retested in duplicate. Repeatedly reactive results will not be invalidated by a failed release control and stay reactive. Other results rendered invalid due to a failed release control result must be retested after resolving the cause for the failed control measurement.

For a valid batch of sample results, the release control is tested at user-defined intervals with a maximum span of every 300 samples or 350 determinations within 24 hours from the PreciControl and must be tested in order to release the test results. Reactive results will not be invalidated. The release control must meet specifications defined in the PreciControl Release HTLV value sheet in order to validate the system functionality and release test results. For troubleshooting information, refer to User Assistance **cobas pro** serology solution or contact US Customer Technical Support.

Calculation

The analytical unit automatically calculates the cutoff based on the measurement of HTLVB Cal1 and HTLVB Cal2.

The result of a sample is given either as reactive or non-reactive as well as in the form of a cutoff index (signal sample/cutoff).

Interpretation of the results

Initial result

Numeric result	Result	Interpretation
COI < 1.00	Non-reactive	Non-reactive for HTLV-I/II-specific antibodies. No further testing needed.
COI ≥ 1.00	Reactive	Reactive in the Elecsys HTLV-I/II assay. All initially reactive samples should be retested in duplicate with the Elecsys HTLV-I/II assay. Redetermination of samples with an initial COI ≥ 1.00 can be performed automatically (see section **cobas e** flow).

Final result

Numeric result	Final result	Interpretation/ further steps
One or both of the duplicate retests have a COI ≥ 1.00	Repeatedly reactive	Repeatedly reactive samples must be confirmed according to supplementary algorithms.
Both of the duplicate retests have a COI < 1.00	Non-reactive	Non-reactive for HTLV-I/II-specific antibodies. No further testing needed.

cobas e flow

A **cobas e** flow is a procedure programmed into the system to enable a fully automated sequence of measurements and the calculation of assay combinations to perform decision algorithms.
A **cobas e** flow is available to perform a repetition of measurements in duplicate automatically for samples with an initial cutoff index ≥ 1.00 (short name HTLVBR).

Limitations of the test

A non-reactive test result does not completely rule out the possibility of an infection with HTLV-I or HTLV-II. Serum or plasma samples from the very early (preseroconversion) phase can occasionally yield non-reactive findings. New HTLV variants can also lead to non-reactive HTLV results.

Specific performance data

Representative performance data is given below. Results obtained in individual laboratories may differ.

Precision

A study was performed based on guidance from CLSI EP05-A3 (n = 84). Testing was conducted at 1 site using 1 lot of the Elecsys HTLV-I/II assay and 1 lot of PreciControl HTLV. Panel members and controls were tested in 4 replicates, 1 run per day for 21 days. The precision and reproducibility for the Elecsys HTLV-I/II assay are presented in the following table.

Overall precision for Elecsys HTLV-I/II

Sample	Mean (COI)	Repeatability SD (COI)	Repeatability % CV	Within-laboratory SD (COI)	Within-laboratory % CV
HSP 01 c)	0.100	0.001	1.2	0.002	1.7
HSP 02	0.968	0.013	1.4	0.023	2.3
HSP 03	0.906	0.012	1.3	0.020	2.2
HSP 04	1.12	0.015	1.3	0.027	2.4
HSP 05	5.88	0.081	1.4	0.165	2.8
HSP 06	25.5	0.477	1.9	0.799	3.1
PC HTLV0 d)	0.101	0.002	2.0	0.002	2.2
PC HTLV1	5.37	0.096	1.8	0.135	2.5
PC HTLV2	2.79	0.045	1.6	0.073	2.6

c) HSP = human specimens

d) PC = PreciControl

Reproducibility

A study was performed based on guidance from CLSI EP05-A3 (n = 270). Testing was conducted at 3 external sites using 3 lots of the Elecsys HTLV-I/II assay and 3 lots of PreciControl HTLV. Panel members and controls were tested in 2 runs per day for 5 days with 3 sample replicates per run. The results for the Elecsys HTLV-I/II assay are presented in the following tables.

Overall repeatability and reproducibility for Elecsys HTLV-I/II

Sample	Mean (COI)	Repeatability SD (COI)	Repeatability CV (%)	Between run SD (COI)	Between run CV (%)
HSP 16	1.97	0.031	1.55	0.017	0.872
HSP 17	9.73	0.144	1.48	0.103	1.06
HSP 18	1.92	0.028	1.44	0.025	1.32

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Sample	Mean (COI)	Repeatability SD (COI)	Repeatability CV (%)	Between run SD (COI)	Between run CV (%)
HSP 19	11.8	0.187	1.58	0.133	1.12
PC HTLV0	0.110	0.002	1.45	0.000	0.000
PC HTLV1	5.07	0.090	1.78	0.086	1.69
PC HTLV2	2.44	0.034	1.40	0.058	2.37

Overall repeatability and reproducibility for Elecsys HTLV-I/II

Sample	Mean (COI)	Between day SD (COI)	Between day CV (%)	Intermediate precision SD (COI)	Intermediate precision CV (%)
HSP 16	1.97	0.016	0.806	0.039	1.95
HSP 17	9.73	0.031	0.318	0.179	1.84
HSP 18	1.92	0.005	0.251	0.038	1.97
HSP 19	11.8	0.065	0.550	0.239	2.02
PC HTLV0	0.110	0.001	0.603	0.002	1.57
PC HTLV1	5.07	0.000	0.000	0.124	2.45
PC HTLV2	2.44	0.009	0.389	0.068	2.77

Overall repeatability and reproducibility for Elecsys HTLV-I/II

Sample	Mean (COI)	Between site SD (COI)	Between site CV (%)	Between lot SD (COI)	Between lot CV (%)
HSP 16	1.97	0.000	0.000	0.074	3.73
HSP 17	9.73	0.030	0.313	0.624	6.41
HSP 18	1.92	0.000	0.000	0.058	3.04
HSP 19	11.8	0.038	0.325	0.299	2.53
PC HTLV0	0.110	0.002	1.41	0.014	12.7
PC HTLV1	5.07	0.000	0.000	0.277	5.46
PC HTLV2	2.44	0.008	0.347	0.093	3.81

Overall repeatability and reproducibility for Elecsys HTLV-I/II

Sample	Mean (COI)	Reproducibility SD (COI)	Reproducibility CV (%)
HSP 16	1.97	0.083	4.21
HSP 17	9.73	0.650	6.68
HSP 18	1.92	0.070	3.62
HSP 19	11.8	0.385	3.25
PC HTLV0	0.110	0.014	12.8
PC HTLV1	5.07	0.303	5.98
PC HTLV2	2.44	0.115	4.72

Results: The precision and reproducibility of the Elecsys HTLV-I/II assay demonstrated minor variability from run to run, day to day and between reagent lots.

Analytical specificity

The effect of the following endogenous substances on assay performance were tested. Interferences were tested up to the listed concentrations and no impact on results was observed.

Endogenous substances

Compound	Concentration tested
Bilirubin	≤ 753 µmol/L or ≤ 44 mg/dL
Hemoglobin	≤ 0.311 mmol/L or ≤ 500 mg/dL
Intralipid	≤ 2000 mg/dL
Biotin	≤ 4912 nmol/L or ≤ 1200 ng/mL
Albumin	≤ 7.0 g/dL

Additionally, naturally elevated samples for bilirubin, rheumatoid factor, triglycerides (lipemic), hemoglobin and albumin were tested; no false reactive results were found.

No false non-reactive result due to high-dose hook effect was found with the Elecsys HTLV-I/II assay.

In rare cases, interference due to extremely high titers of antibodies to immunological components, streptavidin or ruthenium can occur and these effects are minimized by assay formulation and design.

Clinical specificity

A total of 3775 fresh serum specimens and 3902 fresh plasma specimens from volunteer whole blood donors were collected at 3 blood centers. The initial and repeat reactive rates for the serum specimens were 0.19 % (7/3775) and 0.19 % (7/3775), respectively. The initial and repeat reactive rates for the plasma specimens were 0.08 % (3/3902) and 0.08 % (3/3902), respectively. Repeatedly reactive specimens were further tested using a supplemental HTLV immunoblot. Based on supplemental test results, 0 specimens were positive, 6 specimens were negative, and 4 specimens were inconclusive.

Specificity based on assumed zero prevalence of antibody to HTLV-I/HTLV-II in whole blood donors was estimated in this study to be 99.87 % (7667/7677) with a 95 % confidence interval of 99.76 % to 99.93 %.

Specificity of Elecsys HTLV-I/II

Specimen category	Number tested	Number IR e) (% of total)	Number RR f) (% of total)	Number positive by supplemental testing (% of RR)	Specificity (%) g) (95 % CI)
Volunteer blood donors - serum	3775	7 (0.19)	7 (0.19)	0 (0.000)	99.81 3768/3775 (99.62 - 99.91)
Volunteer blood donors - plasma	3902	3 (0.08)	3 (0.08)	0 (0.000)	99.92 3899/3902 (99.77 - 99.97)
Total volunteer blood donors	7677	10 (0.13)	10 (0.13)	0 (0.000)	99.87 7667/7677 (99.76 - 99.93)

e) IR = initially reactive

f) RR = repeatedly reactive

g) Based on supplemental test results for the 10 repeatedly reactive specimens (7 serum and 3 plasma).

Clinical sensitivity

A total of 542 confirmed positive specimens from the categories shown in the table below were tested using the Elecsys HTLV-I/II assay at 3 clinical sites. Repeatedly reactive specimens from individuals at increased risk of HTLV-I/II infection, and individuals from HTLV-I/II endemic areas were tested using a supplemental HTLV immunoblot.

Sensitivity was estimated to be 100 % (542/542) with a 95 % confidence interval of 99.30 % to 100 % for preselected positive specimens.

Reactivity of the Elecsys HTLV-I/II assay in individuals known to be positive for HTLV-I/HTLV-II antibodies and anti-HTLV undifferentiated individuals

Specimen category	Number tested	Number positive	Number RR (% of RR)	Number RR that were positive (% of RR)	Sensitivity (%) (95% CI)
Samples known to be positive for antibodies to HTLV-I	261	261	261 (100)	261 (100)	100 (98.55 - 100)
Samples known to be positive for antibodies to HTLV-II	243	243	243 (100)	243 (100)	100 (98.44 -100)
HTLV Undifferentiated	38	38	38 (100)	38 (100)	100 (90.82 - 100)
Total	542	542	542 (100)	542 (100)	100 (99.30 - 100)

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Reactivity of the Elecsys HTLV-I/II assay in individuals at increased risk for HTLV-I/HTLV-II infection, and from HTLV-I/HTLV-II endemic areas

Specimen category	Number tested	Number Initially Reactive (% of Total)	Number RR (% of Total)	Number Positive by Algorithm Testing (% of RR) h)
Increased Risk for HTLV-I/II	409	9	9 (2.20)	7 (77.78)
Individuals from Endemic Areas i)	802	0	0 (n.a.)	0 (n.a.)

h) The sensitivity calculation and/or confidence interval are not meaningful due to the small number of positive specimens.

i) Individuals from HTLV-I/II endemic areas included specimens from the following areas: El Salvador (200), Argentina (72), Uruguay (158), Paraguay (125), Bolivia (96), and Chile (151).

Other specimen conditions or disease states

248 samples containing potentially interfering substances were tested with the Elecsys HTLV-I/II assay comprising specimens:

- containing antibodies against CMV, EBV, HAMA (Human anti-murine antibody), HAV, HBV (acute and chronic), HCV, HEV, HIV, HSV-1/2, Rubella and VZV.
- containing autoantibodies (ANA) and Heterophilic antibodies
- containing antibodies against *Candida albicans*, *Chlamydia*, *Escherichia coli*, *Toxoplasma gondii* and *Treponema pallidum* (syphilis)
- after vaccination against influenza
- from persons with Hyper IgG and Hyper IgM
- from pregnant women and multiparous pregnancies

Results showed no interference from the above agents.

References

1 Conçalves DU, Proietti FA, Ribas JGR, et al. Epidemiology, Treatment and Prevention of Human T-Cell Leukemia Virus Type 1-Associated Diseases. Clin Microbiol Rev 2010;23(3):577-589.

2 Proietti FA, Carneiro-Proietti AB, Catalan-Soares BC, et al. Global epidemiology of HTLV-I infection and associated diseases. Oncogene 2005;24(39):6058-6068.

3 Manns A, Hisada M, La Grenade L. Human T-lymphotropic virus type I infection. Lancet 1999;353:1951-1958.

4 Hall WW, Takahashi H, Liu C, et al. Multiple isolates and characteristics of human T-cell leukemia virus type II. J Virol 1992;66:2456-2463.

5 Eiraku N, Novoa P, da Costa Ferreira M, et al. Identification and characterization of a new and distinct molecular subtype of human T-cell lymphotropic virus type 2. J Virol 1996;70:1481-1492.

6 Vandamme AM, Salemi M, Van Brussel M, et al. African origin of human T-lymphotropic virus type 2 (HTLV-2) supported by a potential new HTLV-2d subtype in Congolese Bambuti Efe Pygmies. Journal of virology 1998;72(5):4327-4340.

7 Schupbach J. The Human Retroviruses Human Immunodeficiency Virus and Human T-Lymphotropic Virus. Clinical Virology Manual 2009. Washington, DC:American Society for Microbiology.

8 Okochi K, Sato H, Hinuma Y. A retrospective study on transmission of adult T cell leukemia virus by blood transfusion: seroconversion in recipients. Vox Sang 1984;46:245-253.

9 Cook LB, Elemans M, Rowan AG, et al. HTLV-1: Persistence and pathogenesis. Virology 2013;435:131-140.

10 Murphy EL, Wang B, Sacher RA, et al. Respiratory and Urinary Tract Infections, Arthritis, and Asthma Associated with HTLV-I and HTLV-II Infection. Emerg Infect Dis 2004;10:109-116.

11 Zehender G, Colasante C, Santambrogio S, et al. Increased Risk of Developing Peripheral Neuropathy in Patients Coinfected With HIV-1 and HTLV-2. JAIDS 2002;31:440-447.

12 Occupational Safety and Health Standards: Bloodborne pathogens. (29 CFR Part 1910.1030). Fed. Register.

13 Directive 2000/54/EC of the European Parliament and Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work.

For further information, please refer to the appropriate user guide for the analytical unit concerned and the Method Sheets of all necessary components (if available in your country).

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see navifyportal.roche.com for definition of symbols used):

CONTENT	Contents of kit
SYSTEM	Analyzers/Instruments on which reagents can be used
REAGENT	Reagent
CALIBRATOR	Calibrator
→	Volume for reconstitution
GTIN	Global Trade Item Number
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

FOR US CUSTOMERS ONLY: LIMITED WARRANTY

Roche Diagnostics warrants that this product will meet the specifications stated in the labeling when used in accordance with such labeling and will be free from defects in material and workmanship until the expiration date printed on the label. THIS LIMITED WARRANTY IS IN LIEU OF ANY OTHER WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR PARTICULAR PURPOSE. IN NO EVENT SHALL ROCHE DIAGNOSTICS BE LIABLE FOR INCIDENTAL, INDIRECT, SPECIAL OR CONSEQUENTIAL DAMAGES.

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