Elecsys HIV combi PT

cobas®

REF		Σ	SYSTEM
			cobas e 411
08924163190	08924163500	100	**cobas e** 601
			cobas e 602

English

System information

For **cobas e** 411 analyzer: test number 2250
For **cobas e** 601 and **cobas e** 602 analyzers: Application Code Number 225

Intended use

Immunoassay for the in vitro qualitative determination of HIV-1 p24 antigen and antibodies to HIV-1, including group O, and HIV-2 in human serum and plasma.

The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use on **cobas e** immunoassay analyzers.

Summary

The Elecsys HIV combi PT assay is intended to be used as an aid, in conjunction with other laboratory results and clinical information, in the diagnosis of and the screening for HIV infection. In addition, the assay is intended to be used for screening as first-line assay of individual human donors of blood, blood components, cells, tissue, and organs, when donors samples are obtained while the donor´s heart is still beating and of cadaveric blood specimens (specimens collected post-mortem, non-heart-beating). The use of cadaveric blood specimens has been established according to Paul-Ehrlich-Institut (PEI) recommendation.[1]

The human immunodeficiency virus (HIV), the causative agent of Acquired Immunodeficiency Syndrome (AIDS), belongs to the family of retroviruses.[2,3,4] HIV can be transmitted through sexual contact, contaminated blood and blood products or from an HIV-infected mother to her child before, during and after birth.[3,5,6]
Two types of HIV, called HIV-1 and HIV-2, have been identified to date.[4,7,8,9,10]

HIV-1 can be divided into 4 distantly related groups: group M (for main), group N (for non-M, non-O), group O (for outlier) and group P.[3,11,12] Based on their genetic relationship, 10 different subtypes (A to D, F to H, J, K, L) as well as several circulating recombinant forms (CRFs) have been identified within HIV-1 group M.[3,13,14,15,16] The majority of HIV-1 infections worldwide are caused by viruses belonging to group M, while geographical distribution of subtypes and CRFs within this group varies strongly.[17,18] Due to differences in the sequence of immunodominant epitopes, especially in the envelope proteins of HIV-1 group M, HIV-1 group O and HIV-2, specific antigens are necessary to avoid failure in the detection of an HIV infection by immunoassays.[19,20,21]

HIV p24 antigen in blood specimen of recently infected patients can be detected as early as 2-3 weeks after infection.[22,23,24,25] Anti-HIV antibodies are detectable in serum from around 3-4 weeks post infection; the time point of detectability depends on the assay methodology and the individual patient.[21,22,25,26,27,28,29] The combined detection of HIV p24 antigen and anti-HIV antibodies in 4th generation HIV screening assays leads to improved sensitivity and therefore a shorter diagnostic window compared to traditional anti-HIV assays.[21,30,26]

With the Elecsys HIV combi PT assay the HIV-1 p24 antigen and antibodies to HIV-1 and HIV-2 can be detected simultaneously within one determination.[6] The assay uses recombinant antigens derived from the *env*- and *pol*-region of HIV-1 (including group O) and HIV-2 to determine HIV-specific antibodies. For the detection of HIV-1 p24 antigen specific monoclonal antibodies are used. Repeatedly reactive samples must be confirmed according to recommended local testing algorithms which include confirmatory tests like HIV-1/HIV-2 differentiation assays, HIV nucleic acid testing (NAT) and Immunoblot.[21,26,31,32]

Test principle

Sandwich principle. Total duration of assay: 27 minutes.

- 1st incubation: Pretreatment of 40 µL of sample with detergent agent.
- 2nd incubation: Biotinylated monoclonal anti-p24 antibodies/HIV-specific recombinant antigens/HIV-specific peptides, and monoclonal anti-p24 antibodies/HIV-specific recombinant antigens/HIV-specific peptides labeled with a ruthenium complex[a)] react to form a sandwich complex.
- 3rd 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/ProCell 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 reaction product of the sample with the signal of the cutoff value previously obtained by calibration.

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

Reagents - working solutions

The reagent rackpack (M, R0, R1, R2) is labeled as HIVCOMPT.

M Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R0 MES[b)] buffer 50 mmol/L, pH 5.5; 1.5 % Nonylphenol, ethoxylated; preservative (white cap), 1 bottle, 4 mL.

R1 Anti-HIV p24-Ab~, HIV-1/2-specific recombinant antigens (E. coli)~, HIV-1/2-specific peptides~biotin (gray cap), 1 bottle, 7 mL: Biotinylated monoclonal anti-p24 antibodies (mouse), biotinylated HIV-1/2-specific recombinant antigens (E. coli), biotinylated HIV-1/2-specific peptides > 1.3 mg/L; TRIS[c)] buffer 50 mmol/L, pH 7.5; preservative.

R2 Anti-HIV p24-Ab~, HIV-1/2-specific recombinant antigens (E. coli)~, HIV-1/2-specific peptides~$Ru(bpy)_3^{2+}$ (black cap), 1 bottle, 7 mL: Monoclonal anti-p24 antibodies (mouse), HIV-1/2-specific recombinant antigens, HIV-1/2-specific peptides labeled with ruthenium complex > 1.5 mg/L; TRIS buffer 50 mmol/L, pH 7.5; preservative.

b) MES = 2-morpholino-ethane sulfonic acid

c) TRIS = Tris(hydroxymethyl)-aminomethane

HIVCOMPT Cal1 Negative calibrator (white cap; lyophilized), 2 bottles for 1.0 mL each:
Human serum, non reactive for anti-HIV-1 and anti-HIV-2.

HIVCOMPT Cal2 Positive calibrator (black cap; lyophilized), 2 bottles for 1.0 mL each:
Anti-HIV-1 positive human serum (inactivated) in human serum negative for anti-HIV-1 and anti-HIV-2.

Precautions and warnings

For in vitro diagnostic use for laboratory professionals. 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:

Elecsys HIV combi PT

cobas®

Warning

H317	May cause an allergic skin reaction.
H319	Causes serious eye irritation.
H412	Harmful to aquatic life with long lasting effects.

Prevention:

P261	Avoid breathing mist or vapours.
P273	Avoid release to the environment.
P280	Wear protective gloves/ eye protection/ face protection.

Response:

P333 + P313	If skin irritation or rash occurs: Get medical advice/attention.
P337 + P313	If eye irritation persists: Get medical advice/attention.
P362 + P364	Take off contaminated clothing and wash it before reuse.

Hazardous components:

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

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

For customers in the European Economic Area:
Contains SVHC: octyl/nonylphenol ethoxylates.

For use as IVD only – cartridges / rests of product to be disposed of as if it was hazardous waste.

Use as IVD only according to REACH authorization number REACH/23/16/3.

All human material should be considered potentially infectious. All products derived from human blood are 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.[33,34]

The negative calibrator (HIVCOMPT Cal1) has been prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV.

The serum containing anti-HIV-1 (HIVCOMPT Cal2) was inactivated using β-propiolactone and UV-radiation.

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

Reagent handling

The reagents (M, R0, R1, R2) in the kit are ready-for-use and are supplied in bottles compatible with the system.

Calibrators: Carefully dissolve the contents of 1 bottle 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 bottles.

cobas e 411 analyzer: The reconstituted calibrators should only be left on the analyzer during calibration at 20-25 °C. After use, close the bottles as soon as possible and store upright at 2-8 °C.

Due to possible evaporation effects, not more than 5 calibration procedures per calibrator bottle set should be performed.

cobas e 601 and **cobas e** 602 analyzers: Unless the entire volume is necessary for calibration on the analyzers, transfer aliquots of the reconstituted calibrators into empty snap-cap bottles (CalSet Vials). Attach the supplied labels to these additional bottles. Store the aliquots at 2-8 °C for later use.

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

All information required for correct operation is read in from the respective reagent barcodes.

Please note for **cobas e** 602 analyzers: Both the vial labels, and the additional labels (if available) contain 2 different barcodes. Please turn the vial cap 180° into the correct position so that the barcode between the yellow markers can be read by the system. Place the vial on the analyzer as usual.

Storage and stability

Store at 2-8 °C.

Do not freeze.

Store the Elecsys reagent kit **upright** in order to ensure complete availability of the microparticles during automatic mixing prior to use.

Stability of the reagent rackpack	
unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	12 weeks
on the analyzers	28 days

Stability of the calibrators	
lyophilized	up to the stated expiration date
reconstituted at 2-8 °C	12 weeks
on **cobas e** 411 at 20-25 °C	up to 5 hours
on **cobas e** 601 and **cobas e** 602 at 20-25 °C	use only once

Store calibrators **upright** in order to prevent the calibrator solution from adhering to the snap-cap.

Specimen collection and preparation

Specimen collected from living patients, blood donors, or individual organ, tissue or cell donors may be used, including donor samples obtained while the donor's heart is still beating.
Performance for the use of cadaveric blood specimens (specimens collected post-mortem, non-heart-beating) was established according to Paul-Ehrlich-Institut recommendation[35] with samples obtained within 24 hours after death.[36] Qualitative differences of neat (non-reactive) or spiked (reactive) specimens from cadaveric compared to living donors were not observed.

Criterion: Mean value of cadaveric specimens compared to specimens from living donors within a recovery of 75-125 %.

Only the specimens listed below were tested and found acceptable.

Serum collected using standard sampling tubes or tubes containing separating gel.

Li-heparin, Na-heparin, K_2-EDTA, K_3-EDTA, ACD, CPD, CP2D, CPDA and Na-citrate plasma as well as Li-heparin plasma tubes containing separating gel.

Criterion: Correct assignment of negative and positive samples.

Sampling devices containing liquid anticoagulants have a dilution effect resulting in lower cutoff index (COI) values for individual patient specimens.

In order to minimize dilution effects it is essential that respective sampling devices are filled completely according to manufacturer's instructions.

Stability:
For living patients and donor specimens obtained while the donor's heart is still beating: Stable for 7 days at 20-25 °C, 4 weeks at 2-8 °C, 3 months at -20 °C (± 5 °C). The samples may be frozen 5 times.
For cadaveric specimens: Stable for 3 days at 20-25 °C, 7 days at 2-8 °C. The samples may be frozen 3 times.

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.

Centrifuge samples containing precipitates and thawed samples before performing the assay.

Do not use heat-inactivated samples.

Do not use samples and controls stabilized with azide.

Do not use post-mortem samples collected later than 24 hours after last heart beat.

Ensure the samples, calibrators and controls are at 20-25 °C prior to measurement.

Due to possible evaporation effects, samples, calibrators and controls on the analyzers should be analyzed/measured within 2 hours.

The performance of the Elecsys HIV combi PT assay has not been established with body fluids other than serum and plasma.

Specimens should not be subsequently altered with additives (e.g. biocides, anti-oxidants or substances that could possibly change the pH or ionic strength of the sample) in order to avoid erroneous findings.

Materials provided

See "Reagents – working solutions" section for reagents.

- 2 x 4 bottle labels
- 4 empty labeled snap-cap bottles

Materials required (but not provided)

- REF 06924107190, PreciControl HIV Gen II, for 6 x 2.0 mL
- REF 06924115190, PreciControl HIV; HIV-2+GrpO, for 4 x 2.0 mL (optional use)
- REF 11776576322, CalSet Vials, 2 x 56 empty snap-cap bottles
- General laboratory equipment
- **cobas e** analyzer
- Distilled or deionized water

Additional materials for the **cobas e** 411 analyzer:

- REF 11662988122, ProCell, 6 x 380 mL system buffer
- REF 11662970122, CleanCell, 6 x 380 mL measuring cell cleaning solution
- REF 11930346122, Elecsys SysWash, 1 x 500 mL washwater additive
- REF 11933159001, Adapter for SysClean
- REF 11706802001, AssayCup, 60 x 60 reaction cups
- REF 11706799001, AssayTip, 30 x 120 pipette tips
- REF 11800507001, Clean-Liner

Additional materials for **cobas e** 601 and **cobas e** 602 analyzers:

- REF 04880340190, ProCell M, 2 x 2 L system buffer
- REF 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- REF 03023141001, PC/CC-Cups, 12 cups to prewarm ProCell M and CleanCell M before use
- REF 03005712190, ProbeWash M, 12 x 70 mL cleaning solution for run finalization and rinsing during reagent change
- REF 03004899190, PreClean M, 5 x 600 mL detection cleaning solution
- REF 12102137001, AssayTip/AssayCup, 48 magazines x 84 reaction cups or pipette tips, waste bags
- REF 03023150001, WasteLiner, waste bags
- REF 03027651001, SysClean Adapter M

Additional materials for all analyzers:

- REF 11298500316, 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 analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

Resuspension of the microparticles takes place automatically prior to use. Read in the test-specific parameters via the reagent barcode. If in exceptional cases the barcode cannot be read, enter the 15-digit sequence of numbers.

cobas e 601 and **cobas e** 602 analyzers: PreClean M solution is necessary.

Bring the cooled reagents to approximately 20 °C and place on the reagent disk (20 °C) of the analyzer. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the bottles.

Calibrators:

Place the reconstituted calibrators in the sample zone.

All the information necessary for calibrating the assay is automatically read into the analyzer.

After calibration has been performed, store the calibrators at 2-8 °C or discard (**cobas e** 601 and **cobas e** 602 analyzers).

Calibration

Traceability:

Anti-HIV-1 and anti-HIV-2: No internationally accepted standard for anti-HIV-1 and anti-HIV-2 exists. This method has been standardized against a Roche standard. The units have been selected arbitrarily.

HIV-1 p24 antigen: This method has been standardized against the Human Immunodeficiency Virus Type 1 (HIV-1 p24 Antigen) - 1st International Reference Reagent 1992, code 90/636 - available from NIBSC (National Institute for Biological Standards and Control).

Calibration frequency: Calibration must be performed once per reagent lot using HIVCOMPT Cal1, HIVCOMPT Cal2 and fresh reagent (i.e. not more than 24 hours since the reagent kit was registered on the analyzer).

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Renewed calibration is recommended as follows:

- after 1 month (28 days) when using the same reagent lot
- after 7 days (when using the same reagent kit on the analyzer)
- as required: e.g. quality control findings outside the defined limits

Quality control

For quality control, use PreciControl HIV Gen II. The use of PreciControl HIV; HIV-2+GrpO is optional. Note that all HIV results are sufficiently controlled if only PreciControl HIV Gen II is used.

Controls for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per reagent kit, and following each calibration.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

If necessary, repeat the measurement of the samples concerned.

Follow the applicable government regulations and local guidelines for quality control.

Note:
For technical reasons re-assigned target values valid only for a specific reagent and control lot combination must be entered manually on all analyzers (except for the **cobas e** 602 analyzer). Therefore always refer to the value sheet included in the reagent kit or PreciControl kit to make sure that the correct target values are used.
When a new reagent or control lot is used, the analyzer will use the original values encoded in the control barcodes.

Calculation

The analyzer automatically calculates the cutoff based on the measurement of HIVCOMPT Cal1 and HIVCOMPT 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

Samples with a cutoff index < 0.90 are non-reactive in the Elecsys HIV combi PT assay. These samples are considered negative for HIV-1 Ag and HIV-1/-2 specific antibodies and do not need further testing. Samples

Elecsys HIV combi PT

cobas®

having a cutoff index in the range ≥ 0.90 to < 1.0 are considered borderline in the Elecsys HIV combi PT assay.

Samples with a cutoff index ≥ 1.0 are considered reactive in the Elecsys HIV combi PT assay.

All initially reactive or borderline samples should be redetermined in duplicate with the Elecsys HIV combi PT assay. If cutoff index values < 0.90 are found in both cases, the samples are considered negative for HIV-1 Ag and HIV-1/-2 specific antibodies.

Initially reactive or borderline samples giving cutoff index values of ≥ 0.90 in either of the redeterminations are considered repeatedly reactive. Repeatedly reactive samples must be confirmed according to recommended local testing algorithms which include confirmatory tests like HIV-1/HIV-2 differentiation assays, HIV nucleic acid testing (NAT) and Immunoblot.[21,26,31,32]

Limitations - interference

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

Endogenous substances

Compound	Concentration tested
Bilirubin	≤ 1026 µmol/L or ≤ 60 mg/dL
Hemoglobin	≤ 0.310 mmol/L or ≤ 500 mg/dL
Intralipid	≤ 1500 mg/dL
Biotin	≤ 4912 nmol/L or ≤ 1200 ng/mL
Rheumatoid factors	≤ 1500 IU/mL

Criterion: Correct assignment of negative and positive samples.

No false negative result due to high-dose hook effect was found with the Elecsys HIV combi PT assay.

Pharmaceutical substances
In vitro tests were performed on 18 commonly used pharmaceuticals. No interference with the assay was found.

In rare cases, interference due to extremely high titers of antibodies to analyte-specific antibodies, streptavidin or ruthenium can occur. These effects are minimized by suitable test design.

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

A negative test result does not completely rule out the possibility of an infection with HIV. Serum or plasma samples from the very early (pre-seroconversion) phase or the late phase of HIV infection can occasionally yield negative findings. Yet unknown HIV variants can also lead to a negative HIV finding. The presence of HIV antigen or antibodies to HIV is not a diagnosis of AIDS.

Limits and ranges

Antigen detection

Detection limit: ≤ 2 IU/mL

The stated sensitivity was determined by reading off the HIV Ag concentration corresponding to the signal of the cutoff value from standard curves obtained by serial dilutions of the Human Immunodeficiency Virus Type 1 (HIV-1 p24 Antigen) - 1st International Reference Reagent 1992, code 90/636 - in human HIV-negative serum.

Antibody detection

No internationally accepted standard for HIV-specific antibody detection exists.

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined using Elecsys reagents, samples and controls in a protocol (EP05-A3) of the CLSI (Clinical and Laboratory Standards Institute): 2 runs per day in duplicate each for 21 days (n = 84). The following results were obtained:

cobas e 411 analyzer					
		Repeatability[d]		**Intermediate precision**[e]	
Sample	Mean COI	SD COI	CV %	SD COI	CV %
HS[f], negative	0.141	0.022	-	0.041	-
HS, positive for HIV Ag	1.65	0.040	2.4	0.058	3.5
HS, positive for anti-HIV-1	1.85	0.044	2.4	0.056	3.0
HS, positive for anti-HIV-1	41.7	0.602	1.4	0.861	2.1
HS, positive for anti-HIV-2	1.80	0.044	2.4	0.065	3.6
HS, positive for anti-HIV-1 group O	1.63	0.034	2.1	0.060	3.7
PreciControl HIV1	0.205	0.020	-	0.036	-
PreciControl HIV2	4.66	0.074	1.6	0.103	2.2
PreciControl HIV3	4.55	0.065	1.4	0.124	2.7
PreciControl HIV4	4.25	0.062	1.5	0.080	1.9
PreciControl HIV5	4.99	0.101	2.0	0.118	2.4

d) Repeatability = within-run precision

e) Intermediate precision = between-run

f) HS = human serum

cobas e 601 and **cobas e** 602 analyzers					
		Repeatability		**Intermediate precision**	
Sample	Mean COI	SD COI	CV %	SD COI	CV %
HS, negative	0.104	0.007	-	0.010	-
HS, positive for HIV Ag	1.65	0.037	2.2	0.047	2.9
HS, positive for anti-HIV-1	1.93	0.045	2.3	0.057	3.0
HS, positive for anti-HIV-1	46.0	0.762	1.7	0.995	2.2
HS, positive for anti-HIV-2	1.94	0.054	2.8	0.070	3.6
HS, positive for anti-HIV-1 group O	1.79	0.037	2.1	0.056	3.2
PreciControl HIV1	0.163	0.009	-	0.011	-
PreciControl HIV2	4.85	0.090	1.9	0.120	2.5
PreciControl HIV3	4.52	0.088	1.9	0.115	2.5
PreciControl HIV4	4.57	0.090	2.0	0.133	2.9
PreciControl HIV5	4.74	0.089	1.9	0.127	2.7

Analytical specificity

1182 samples containing potentially interfering substances were tested with the Elecsys HIV combi PT assay comprising specimens:

- containing antibodies against HAV, HBV, HCV, HTLV, CMV, EBV, HSV, VZV, Toxoplasma gondii, Treponema pallidum, Borrelia, Parvovirus B19
- containing autoantibodies and elevated titers of rheumatoid factor
- positive for Candida, E. coli, Plasmodium falciparum/vivax, Mycobacterium tuberculosis
- after vaccination against HAV, HBV, and influenza
- from patients with monoclonal gammopathy and multiple myeloma/lymphoma

Elecsys HIV combi PT

cobas®

	N	Elecsys HIV combi PT assay		Western Blot[g)]	Analytical specificity
		IR[h)] COI ≥ 1	RR[i)] COI ≥ 1		
Specimens containing potentially interfering substances	1182	1[j)]	1	0	99.92 % 95 % lower confidence limit: 99.53 %

g) Western Blot confirmed positive/indeterminate

h) IR = initially reactive

i) RR = repeatedly reactive

j) Patients with monoclonal gammopathy: 1 out of 21

Clinical sensitivity

Of 1534 samples from HIV infected patients in different stages of the disease and infected with HIV-1 group M, N, O, P and HIV-2, 1534 were found to be reactive with the Elecsys HIV combi PT assay. The sensitivity of the Elecsys HIV combi PT assay in this study was 100 %.

The 95 % lower confidence limit was 99.76 %.

Group	N	Reactive
HIV-1 infected persons from various stages of disease	338	338
Infection with HIV-1 group M (subtypes A-J)	629	629
Infection with HIV-1 group N	1	1
Infection with HIV-1 group O	8	8
Infection with HIV-1 group P	1	1
Infection with HIV-2	472	472
HIV Ag positive specimens	85	85

56 lysates of cell culture supernatants including different HIV-1 group M subtypes (A-H), HIV-1 group N, O, P and HIV-2 were tested and found reactive in the Elecsys HIV combi PT assay.

Seroconversion panels

Seroconversion sensitivity of the Elecsys HIV combi PT assay has been shown by testing 102 commercial seroconversion panels in comparison to registered HIV combi assays or anti-HIV immunoassays and/or HIV Ag assays.

Of 179 HIV samples from early seroconversion phase (according to CS definition), 172 samples were found positive with the Elecsys HIV combi PT assay.

In 46 follow ups of very early HIV infections, 100 out of 105 samples were detected positive with the Elecsys HIV combi PT assay.

Clinical specificity

In a group of 7343 randomly selected blood donors from Europe and Asia the specificity of the Elecsys HIV combi PT assay was found 99.88 % (RR). The 95 % lower confidence limit was 99.77 %.

In a group of 4103 samples from unselected daily routine, dialysis patients and pregnant women the specificity of the Elecsys HIV combi PT assay was found 99.80 % (RR). The 95 % lower confidence limit was 99.61 %.

	N	Elecsys HIV combi PT assay		Western Blot[k)]	Clinical specificity (95 % lower confidence limit)
		IR COI ≥ 1	RR COI ≥ 1		
Blood donors	7343	13	11	1/1	99.88 % (99.77 %)
Unselected samples from daily routine	2721	33	33	26	99.74 % (99.47 %)
Dialysis patients	251	1	1	0	99.60 % (97.80 %)
Pregnant women	1131	1	1	1	100 % (99.67 %)

k) Western Blot confirmed positive/indeterminate. Samples with indeterminate WB were excluded from calculation.

References

1 Proposal for the Validation of Anti-HIV-1/2 or HIV Ag/Ab Combination Assays, anti-HCV-Assays, HBsAg and Anti-HBc assays for Use with Cadaveric Samples; PEI 08/05/2014.

2 Kang Y, Guo J, Chen Z. Closing the door to human immunodeficiency virus. Protein & cell. 2013;4(2):86-102.

3 Armstrong WS, Guarner J, Kraft CS, et al. Human Immunodeficiency Virus. Microbiology spectrum. 2016;4(4).

4 Peeters M, Jung M, Ayouba A. The origin and molecular epidemiology of HIV. Expert review of anti-infective therapy. 2013;11(9):885-96.

5 Deeks SG, Overbaugh J, Phillips A, et al. HIV infection. Nature reviews Disease primers. 2015;1:15035.

6 Vallefuoco L, Mazzarella C, Portella G. Fourth generation assays for HIV testing. Expert Rev Mol Diagn. 2016;16(7):723-32.

7 Barre-Sinoussi F, Chermann JC, Rey F, et al. Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). Science. 1983;220(4599):868-71.

8 Popovic M, Sarngadharan MG, Read E, et al. Detection, isolation, and continuous production of cytopathic retroviruses (HTLV-III) from patients with AIDS and pre-AIDS. Science. 1984;224(4648):497-500.

9 Gallo RC, Salahuddin SZ, Popovic M, et al. Frequent detection and isolation of cytopathic retroviruses (HTLV-III) from patients with AIDS and at risk for AIDS. Science. 1984;224(4648):500-3.

10 Clavel F, Guetard D, Brun-Vezinet F, et al. Isolation of a new human retrovirus from West African patients with AIDS. Science. 1986;233(4761):343-6.

11 Sharp PM, Hahn BH. Origins of HIV and the AIDS pandemic. Cold Spring Harb Perspect Med. 2011;1(1):a006841.

12 Plantier JC, Leoz M, Dickerson JE, et al. A new human immunodeficiency virus derived from gorillas. Nat Med. 2009;15(8):871-2.

13 Hemelaar J. The origin and diversity of the HIV-1 pandemic. Trends Mol Med. 2012;18(3):182-92.

14 Worobey M, Gemmel M, Teuwen DE, et al. Direct evidence of extensive diversity of HIV-1 in Kinshasa by 1960. Nature. 2008;455(7213):661-4.

15 Robertson DL, Anderson JP, Bradac JA, et al. HIV-1 nomenclature proposal. Science. 2000;288(5463):55-6.

16 Yamaguchi J, Vallari A, McArthur C, et al. Brief Report: Complete Genome Sequence of CG-0018a-01 Establishes HIV-1 Subtype L. J Acquir Immune Defic Syndr. 2020;83(3):319-22.

17 Taylor BS, Hammer SM. The challenge of HIV-1 subtype diversity. N Engl J Med. 2008;359(18):1965-6.

18 Bbosa N, Kaleebu P, Ssemwanga D. HIV subtype diversity worldwide. Curr Opin HIV AIDS. 2019;14(3):153-60.

19 Denis F, Leonard G, Sangare A, et al. Comparison of 10 enzyme immunoassays for detection of antibody to human immunodeficiency virus type 2 in West African sera. Journal of clinical microbiology. 1988;26(5):1000-4.

20 Gurtler L. Difficulties and strategies of HIV diagnosis. Lancet. 1996;348(9021):176-9.

21 Centers for Disease Prevention and Control (CDC). Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations, 2014. Available at: https://stacks.cdc.gov/view/cdc/23447. Accessed 07 October 2021.

Elecsys HIV combi PT

cobas®

22 Fiebig EW, Wright DJ, Rawal BD, et al. Dynamics of HIV viremia and antibody seroconversion in plasma donors: implications for diagnosis and staging of primary HIV infection. AIDS. 2003;17(13):1871-9.

23 Busch MP, Lee LL, Satten GA, et al. Time course of detection of viral and serologic markers preceding human immunodeficiency virus type 1 seroconversion: implications for screening of blood and tissue donors. Transfusion. 1995;35(2):91-7.

24 Masciotra S, McDougal JS, Feldman J, et al. Evaluation of an alternative HIV diagnostic algorithm using specimens from seroconversion panels and persons with established HIV infections. J Clin Virol. 2011;52 Suppl 1:S17-22.

25 Hurt CB, Nelson JAE, Hightow-Weidman LB, et al. Selecting an HIV Test: A Narrative Review for Clinicians and Researchers. Sexually transmitted diseases. 2017;44(12):739-46.

26 World Health Organization (WHO). Consolidated guidelines on HIV testing services. 2019. ISBN 978-92-4-155058-1. Available at: https://www.who.int/publications/i/item/978-92-4-155058-1. Accessed 07 October 2021.

27 Kleinman S, Busch MP, Korelitz JJ, et al. The incidence/window period model and its use to assess the risk of transfusion-transmitted human immunodeficiency virus and hepatitis C virus infection. Transfusion medicine reviews. 1997;11(3):155-72.

28 Busch MP, Satten GA. Time course of viremia and antibody seroconversion following human immunodeficiency virus exposure. Am J Med. 1997;102(5B):117-24; discussion 25-6.

29 Petersen LR, Satten GA, Dodd R, et al. Duration of time from onset of human immunodeficiency virus type 1 infectiousness to development of detectable antibody. The HIV Seroconversion Study Group. Transfusion. 1994;34(4):283-9.

30 Weber B. Screening of HIV infection: role of molecular and immunological assays. Expert Rev Mol Diagn. 2006;6(3):399-411.

31 Gokengin D, Geretti AM, Begovac J, et al. 2014 European Guideline on HIV testing. International journal of STD & AIDS. 2014;25(10):695-704.

32 CLSI. Criteria for Laboratory Testing and Diagnosis of Human Immunodeficiency Virus Infections; Approved Guideline. Wayne, PA: Clinical and Laboratory Standards Institute; 2011. CLSI document M53-A.

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

34 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.

35 Proposal for the Validation of Anti-HIV-1/2 or HIV Ag/Ab Combination Assays, anti-HCV-Assays, HBsAg and Anti-HBc assays for Use with Cadaveric Samples; PEI 08/05/2014.

36 Commission Directive 2006/17/EC of 8 February 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells.

For further information, please refer to the appropriate user guide or operator's manual for the analyzer concerned, the respective application sheets and the Method Sheets of all necessary components (if available in your country).

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

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.

The Summary of Safety & Performance Report can be found here: https://ec.europa.eu/tools/eudamed

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

CE 0123

Roche Diagnostics GmbH
Sandhofer Strasse 116
68305 Mannheim, Germany
www.roche.com
+800 5505 6606

Roche