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Materials provided

REF			IVD	Rx only	SYSTEM
08836973162	08836973502	10 x 300			cobas pro serology solution

- 8 empty labeled snap-cap vials

For reagents, refer to the "Reagents" section.

Materials required (but not provided)

REF	Description
06924107162	PreciControl HIV Gen II, 6 x 2.0 mL
06924115162	PreciControl HIV; HIV-2+GrpO, for 4 x 2.0 mL
09367101190	PreciControl Release HIV Gen II, 6 x 2.0 mL
	General laboratory equipment
	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.
	Distilled or deionized water

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

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

For use in the USA only

System information

Short name	ACN (application code number)	Assay type	To be used for
HIVDUOB	12510	cobas e flow	HIV Duo
HIVDUOBR	12511	cobas e flow	HIV Duo duplicate repeat
HIVAGB ^{A)}	11511	HIV Antigen (HIV Ag) embedded application	HIV Duo cobas e flow
AHIVB ^{A)}	11510	Anti-HIV embedded application	HIV Duo cobas e flow

A) Embedded application within HIV Duo

Intended use

Elecsys HIV Duo is an in vitro immunoassay for the simultaneous qualitative detection and differentiation of HIV-1 p24 antigen and antibodies to HIV, HIV-1 (groups M and O) and HIV-2 in human serum and plasma. Elecsys HIV Duo is intended to screen individual human donors, including volunteer donors of whole blood, blood components and source plasma. 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 and in testing serum specimens to screen cadaveric donors when specimens are obtained after the donor's heart has stopped beating.

It is not intended for use on cord blood specimens.

The electrochemiluminescence immunoassay "ECLIA" is intended for use with the **cobas pro** serology solution equipped with a **cobas e** 801 analytical unit.

Summary

The human immunodeficiency virus (HIV), the causative agent of Acquired ImmunoDeficiency Syndrome (AIDS), belongs to the family of retroviruses. 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.

Two types of HIV, called HIV-1 and HIV-2, have been identified to date.^{1,2,3,4} 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 (Plantier).^{5,6,7} Based on their genetic relationship, 10 different subtypes (A to D, F to H, J, K and L) as well as several circulating recombinant forms (CRFs) have been identified within HIV-1 group M.^{8,9} The large majority of HIV-1 infections are caused by viruses belonging to group M, while geographical distribution of subtypes and CRFs within this group varies strongly.¹⁰ 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.^{11,12}

HIV p24 antigen in blood specimens of recently infected patients can be detected as early as 2-3 weeks after infection.^{13,14} Anti-HIV antibodies are detectable in serum from around 4 weeks post infection.^{13,15} The combined detection of HIV p24 antigen and anti-HIV antibodies in fourth generation HIV screening assays leads to improved sensitivity compared to traditional anti-HIV assays.^{16,17}

With the Elecsys HIV Duo assay, HIV-1 p24 antigen (HIV Ag), as well as antibodies to HIV-1 and HIV-2 (anti-HIV) can be detected in parallel with 2 separate determinations. On the basis of these determinations, the Elecsys HIV Duo main result is subsequently calculated automatically by the analytical unit. The subresults HIV Ag and anti-HIV can be used as an aid in the selection of the confirmation algorithm for reactive samples. The Elecsys HIV Duo assay uses monoclonal antibodies to detect the HIV Ag and recombinant antigens derived from the Env- and Pol-region of HIV-1 (including group O) and HIV-2 to detect anti-HIV antibodies.

Test principle

Sandwich principle. Total duration of assay: 18 minutes.

- First incubation: For HIV Ag detection (HIVAGB), 30 µL of sample react with biotinylated monoclonal anti-p24 antibodies and ruthenylated^{a)} monoclonal anti-p24 antibodies, to form a sandwich complex. For anti-HIV detection (AHIVB), 30 µL of sample react with biotinylated HIV-specific recombinant antigens/peptides and ruthenylated^{a)} HIV-specific recombinant antigens/peptides, to form a sandwich complex. The incubations are performed in parallel in separate vessels.
- Second incubation: After streptavidin-coated microparticles have been added, 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 HIV Ag embedded and anti-HIV embedded calibrations. The Elecsys HIV Duo result is calculated automatically based on signal to cutoff ratios (cutoff index, COI) from HIV Ag and anti-HIV.

a) Tris(2,2'-bipyridyl)ruthenium(II)-complex (Ru(bpy)₃²⁺)

Reagents

The **cobas** e pack HIV Ag (M, R1, R2) is labeled as HIVAGB.

The **cobas** e pack Anti-HIV (M, R1, R2) is labeled as AHIVB.

HIVAGB

M	Streptavidin-coated microparticles, 1 bottle, 14.1 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.
R1	Anti-HIV p24-Ab~biotin, 1 bottle, 14.8 mL: Biotinylated monoclonal anti-HIV p24 antibodies (mouse) approximately 0.75 mg/L; MES ^{A)} buffer 50 mmol/L, pH 6.5; preservative.
R2	Anti-HIV p24-Ab~Ru(bpy) ₃ ²⁺ , 1 bottle, 14.8 mL: Monoclonal anti-p24 antibodies (mouse) labeled with ruthenium complex approximately 0.75 mg/L; MES buffer 50 mmol/L, pH 6.5; preservative.
HIVDUOB Cal1	Non-reactive calibrator 1 (lyophilized), 2 vials each for 1.0 mL: Human serum, non-reactive for anti-HIV-1 and anti-HIV-2; preservative
HIVDUOB Cal2	Reactive calibrator 2 (lyophilized), 2 vials each for 1.0 mL: HIV p24 antigen (<i>E. coli</i> , rDNA) in human serum, non-reactive for anti-HIV-1 and anti-HIV-2; preservative.

A) MES = 2-morpholino-ethane sulfonic acid

AHIVB

M	Streptavidin-coated microparticles, 1 bottle, 14.1 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.
R1	HIV-1/2-specific recombinant antigens (<i>E. coli</i>)-biotin, HIV-1/2-specific synthetic peptides~biotin, 1 bottle, 14.8 mL: Biotinylated HIV-1/2-specific recombinant antigens (<i>E. coli</i>) and biotinylated HIV-1/2-specific synthetic peptides approximately 0.63 mg/L; TES ^A buffer 40 mmol/L, pH 7.3; preservative.
R2	HIV-1/2-specific recombinant antigens (<i>E. coli</i>)-Ru(bpy) ₃ ²⁺ , HIV-1/2-specific synthetic peptides~Ru(bpy) ₃ ²⁺ , 1 bottle, 14.8 mL: HIV-1/2-specific recombinant antigens (<i>E. coli</i>) and HIV-1/2-specific synthetic peptides labeled with ruthenium complex approximately 1.22 mg/L; TES buffer 40 mmol/L, pH 7.3; preservative.
HIVDUOB Cal3	Non-reactive calibrator 3 (lyophilized), 2 vials each for 1.0 mL: Human serum, non-reactive for anti-HIV-1 and anti-HIV-2; preservative.
HIVDUOB Cal4	Reactive calibrator 4 (lyophilized), 2 vials each for 1.0 mL: Anti-HIV-1 reactive human serum (inactivated) in human serum non-reactive for anti-HIV-1 and anti-HIV-2; preservative.

A) TES = 2-[[1,3-dihydroxy-2-(hydroxymethyl)propane-2-yl]amino]ethanesulfonic acid

Warnings and precautions

For in vitro diagnostic use.

This test is not intended for use as an aid in diagnosis of HIV-1/HIV-2 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 safe disposal.

The Safety Data Sheet is available for professional users 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 mist or vapours.
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.
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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 non-reactive calibrators (HIVDUOB Cal1 and HIVDUOB Cal3) as well as the HIV Ag reactive calibrator (HIVDUOB 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).

The serum containing anti HIV-1 (HIVDUOB Cal4) was inactivated using β -propiolactone and UV-radiation.

However, as no inactivation or 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 donor specimen. In the event of exposure, the directives of the responsible health authorities should be followed.^{18,19}

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

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.

Calibration

Traceability:

HIVAGB: This method has been standardized against the WHO International Standard HIV-1-p24 Antigen, NIBSC (National Institute for Biological Standards and Control) code 90/636.

AHIVB: No internationally accepted standard for anti-HIV-1 and anti-HIV-2 exists.

Calibration frequency: Calibration must be performed once per reagent lot using HIVDUOB Cal1, HIVDUOB Cal2, HIVDUOB Cal3, HIVDUOB Cal4 and fresh reagent (i.e. not more than 24 hours after the **cobas e** pack was registered on the analytical unit).

Recalibration is required as follows:

- every 12 weeks when using the same reagent lot
- every 28 days when using the same **cobas e** pack on the analytical unit
- as required, such as when quality control findings are outside the defined limits

Quality control

For quality control, use PreciControl HIV Gen II and PreciControl HIV; HIV-2+GrpO.

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 HIV Gen II and PreciControl HIV; HIV-2+GrpO 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 HIV Gen II.

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 HIV Gen II 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.

Specimen collection and preparation

Only the specimens listed below were tested and found acceptable.

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

Serum and Li-heparin, K2 EDTA, K3 EDTA, CPD and Na-citrate plasma collected using standard sampling tubes.

Serum and Li-heparin and K2 EDTA plasma collected in tubes containing separating gel.

Samples on-the-clot are stable for 7 days at 15-30 °C and 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.

Cadaveric samples off-the-clot are stable for 3 days at 15-30 °C, 14 days at 2-8 °C, and 1 month at -20 °C (± 5 °C). Samples off-the-clot may be frozen up to 5 times.

Specimens collected by plasmapheresis, which have not been frozen, do not require centrifugation. All other 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. Not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials that 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 the Elecsys HIV Duo assay has not been established with body fluids other than serum and plasma or with cadaveric plasma specimens.

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

Test procedure

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

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.

Calibrators

Carefully dissolve the contents of 1 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.

Read in all the information necessary for calibrating the assay.

Perform **only 1** calibration procedure per vial.

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

Place the reconstituted calibrators in the sample zone.

Calculation

The analytical unit automatically calculates the cutoff based on the measurement of HIVDUOB Cal1 and HIVDUOB Cal2 for the HIVAGB module, and HIVDUOB Cal3 and HIVDUOB Cal4 for the AHIVB module.

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).

The following formula is used to calculate the main Elecsys HIV Duo result based on the HIVAGB and AHIVB subresults:

$$\text{HIVDUOB (COI)} = \sqrt{(\text{HIVAGB [COI]})^2 + (\text{AHIVB [COI]})^2}$$

Interpretation of results (HIVDUOB or HIVDUOBR)**Initial main result**

Numeric result	Result	Interpretation
COI < 1.00	Non-reactive	Non-reactive for HIV-1 Ag and non-reactive for anti-HIV-1/2 antibodies. No further testing needed.
COI ≥ 1.00	Reactive	Reactive in the Elecsys HIV Duo assay. All initially reactive samples should be retested in duplicate with the Elecsys HIV Duo assay. Redetermination of samples with an initial COI ≥ 1.00 can be performed automatically (see section cobas e flow).

Subresult HIVAGB

Numeric result	Result	Interpretation
COI < 1.00	Non-reactive	Non-reactive for HIV-1 p24 antigen.
COI ≥ 1.00	Reactive	Reactive in the HIV-1 Ag module.

Subresult AHIVB

Numeric result	Result	Interpretation
COI < 1.00	Non-reactive	Non-reactive for anti-HIV-1/2 antibodies.
COI ≥ 1.00	Reactive	Reactive in the anti-HIV module.

Final result

Numeric result	Final result	Interpretation / further steps
Both of the duplicate retests have a COI < 1.00	Non-reactive	Non-reactive for HIV-1 Ag and non-reactive for anti HIV-1/2 antibodies. No further testing needed.
One or both of the duplicate retests have a COI ≥ 1.00	Repeatedly reactive	Repeatedly reactive samples must be confirmed according to supplementary algorithms. The subresults for either HIVAGB or AHIVB can be used as an aid in the selection of the confirmation algorithm for reactive samples.

Please note: In cases where the HIVAGB and AHIVB results are both non-reactive with high negative results near the cutoff, the formula may result in an Elecsys HIV Duo result with a COI ≥ 1.00 and reported as reactive. These results will be flagged as "Antigen test negative, Antibody test negative" and considered as reactive and should be retested in duplicate with the Elecsys HIV Duo assay.

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.

The HIVDUOB **cobas e flow** is required to enable simultaneous separate measurement of HIVAGB and AHIVB with subsequent calculation of the main result.

A second HIV **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 HIVDUOBR). Both subresults and the overall result message will be reported.

Limitations of the test

A non-reactive test result does not 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 non-reactive findings. Yet unknown HIV variants can also lead to non-reactive HIV findings.

False reactive results may be observed due to non-specific interactions.

The detection of HIV-1 p24 antigen or HIV-1/HIV-2 antibodies is not a diagnosis of HIV.

It is recommended that repeatedly reactive specimens be confirmed by supplemental testing. Refer individuals who are repeatedly reactive for medical evaluation, that may include additional testing.

The performance of the Elecsys HIV Duo assay has not been established with body fluids other than serum and plasma or with cadaveric plasma specimens.

Testing of cadaveric serum specimens from patients with plasma dilution due to transfusions of > 2000 mL of blood or colloids within 48 hours, or > 2000 mL of crystalloids within 1 hour (or any combination thereof) prior to collection of the specimens has not been verified.

Specific performance data

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

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 HIV Duo assay and 1 lot each of PreciControl HIV Gen II, PreciControl HIV; HIV-2+GrpO and PreciControl Release HIV Gen II. Panel members and controls were tested in 2 runs per day for 5 days with 3 sample replicates per run. The precision and reproducibility for the Elecsys HIV Duo assay are presented in the following tables.

Overall repeatability and reproducibility for Elecsys HIV Duo (Main result)

Sample	Mean	Repeatability	Repeatability	Between run	Between run	Between day	Between day	Intermediate precision	Intermediate precision
	(COI)	SD (COI)	% CV	SD (COI)	% CV	SD (COI)	% CV	SD (COI)	% CV
HSP ^{A)} 01	2.71	0.036	1.32	0.017	0.630	0.041	1.53	0.057	2.12
HSP 02	22.3	0.313	1.41	0.185	0.832	0.286	1.29	0.463	2.08
HSP 03	2.61	0.035	1.34	0.027	1.02	0.036	1.39	0.057	2.19
HSP 04	22.4	0.269	1.20	0.176	0.784	0.441	1.97	0.546	2.44
HSP 05	2.63	0.041	1.56	0.022	0.819	0.046	1.75	0.065	2.48
HSP 06	3.09	0.048	1.54	0.022	0.704	0.039	1.27	0.066	2.12
HSP 07	26.4	0.353	1.34	0.191	0.725	0.402	1.52	0.568	2.15
PC ^{B)} HIV1 B	0.185	0.021	11.6	0.002	0.849	0.008	4.20	0.023	12.3
PC HIV2 B	3.62	0.058	1.60	0.047	1.31	0.047	1.30	0.088	2.44
PC HIV3 B	9.00	0.103	1.14	0.118	1.31	0.120	1.33	0.197	2.19
PC HIV4 B	4.12	0.071	1.74	0.046	1.12	0.064	1.56	0.107	2.59
PC HIV5 B	5.96	0.114	1.92	0.084	1.40	0.062	1.05	0.155	2.60

A) HSP = human specimens

B) PC = PreciControl

Overall repeatability and reproducibility for Elecsys HIV Duo (Main result)

Sample	Mean	Between site	Between site	Between lot	Between lot	Reproducibility	Reproducibility
	(COI)	SD (COI)	% CV	SD (COI)	% CV	SD (COI)	% CV
HSP 01	2.71	0.000	0.000	0.055	2.03	0.080	2.94
HSP 02	22.3	0.168	0.753	0.747	3.36	0.895	4.02
HSP 03	2.61	0.006	0.244	0.187	7.18	0.196	7.51
HSP 04	22.4	0.000	0.000	0.368	1.64	0.658	2.94
HSP 05	2.63	0.000	0.000	0.052	1.97	0.083	3.17
HSP 06	3.09	0.041	1.34	0.103	3.33	0.129	4.17
HSP 07	26.4	0.260	0.986	0.802	3.04	1.02	3.86
PC HIV1 B	0.185	0.004	2.35	0.017	8.97	0.028	15.4
PC HIV2 B	3.62	0.000	0.000	0.099	2.74	0.133	3.67
PC HIV3 B	9.00	0.062	0.688	0.246	2.73	0.321	3.56
PC HIV4 B	4.12	0.002	0.037	0.217	5.28	0.242	5.88
PC HIV5 B	5.96	0.078	1.30	0.129	2.16	0.216	3.62

Overall repeatability and reproducibility for Elecsys HIV Duo (HIVAGB module)

Sample	Mean	Repeatability	Repeatability	Between run	Between run	Between day	Between day	Intermediate precision	Intermediate precision
	(COI)	SD (COI)	% CV	SD (COI)	% CV	SD (COI)	% CV	SD (COI)	% CV
HSP 01	0.160	0.010	6.10	0.001	0.400	0.006	3.55	0.011	7.07
HSP 02	0.160	0.008	5.25	0.003	2.06	0.007	4.66	0.012	7.32
HSP 03	0.158	0.009	5.85	0.002	1.20	0.007	4.52	0.012	7.49
HSP 04	0.160	0.009	5.49	0.001	0.871	0.007	4.54	0.011	7.18
HSP 05	0.160	0.009	5.53	0.003	1.88	0.007	4.31	0.012	7.26

Elecsys HIV Duo



Sample	Mean	Repeatability	Repeatability	Between run	Between run	Between day	Between day	Intermediate precision	Intermediate precision
	(COI)	SD (COI)	% CV	SD (COI)	% CV	SD (COI)	% CV	SD (COI)	% CV
HSP 06	3.09	0.047	1.53	0.023	0.733	0.040	1.28	0.066	2.13
HSP 07	26.4	0.353	1.34	0.191	0.725	0.402	1.52	0.568	2.15
PC HIV1 B	0.169	0.010	6.06	0.000	0.000	0.007	4.40	0.013	7.49
PC HIV2 B	0.165	0.011	6.62	0.000	0.000	0.006	3.92	0.013	7.69
PC HIV3 B	9.00	0.103	1.14	0.118	1.31	0.120	1.33	0.197	2.19
PC HIV4 B	0.165	0.010	5.78	0.000	0.000	0.006	3.88	0.011	6.96
PC HIV5 B	0.167	0.009	5.59	0.002	1.50	0.007	4.10	0.012	7.09

Overall repeatability and reproducibility for Elecsys HIV Duo (HIVAGB module)

Sample	Mean	Between site	Between site	Between lot	Between lot	Reproducibility	Reproducibility
	(COI)	SD (COI)	% CV	SD (COI)	% CV	SD (COI)	% CV
HSP 01	0.160	0.004	2.65	0.014	8.48	0.018	11.4
HSP 02	0.160	0.006	4.03	0.014	8.84	0.019	12.2
HSP 03	0.158	0.005	3.40	0.013	8.37	0.019	11.7
HSP 04	0.160	0.005	3.14	0.014	8.81	0.019	11.8
HSP 05	0.160	0.004	2.70	0.014	8.89	0.019	11.8
HSP 06	3.09	0.041	1.34	0.103	3.33	0.129	4.17
HSP 07	26.4	0.260	0.986	0.802	3.04	1.02	3.86
PC HIV1 B	0.169	0.007	4.10	0.016	9.66	0.022	12.9
PC HIV2 B	0.165	0.005	3.18	0.017	10.5	0.022	13.4
PC HIV3 B	9.00	0.062	0.688	0.246	2.73	0.321	3.56
PC HIV4 B	0.165	0.007	4.02	0.017	10.3	0.022	13.1
PC HIV5 B	0.167	0.005	2.74	0.018	10.5	0.022	13.0

Overall repeatability and reproducibility for Elecsys HIV Duo (AHIVB module)

Sample	Mean	Repeatability	Repeatability	Between run	Between run	Between day	Between day	Intermediate precision	Intermediate precision
	(COI)	SD (COI)	% CV	SD (COI)	% CV	SD (COI)	% CV	SD (COI)	% CV
HSP 01	2.70	0.036	1.33	0.017	0.616	0.041	1.53	0.057	2.11
HSP 02	22.3	0.314	1.41	0.184	0.829	0.287	1.29	0.464	2.08
HSP 03	2.60	0.035	1.34	0.026	1.02	0.036	1.39	0.057	2.18
HSP 04	22.4	0.270	1.21	0.175	0.782	0.442	1.97	0.547	2.44
HSP 05	2.62	0.041	1.58	0.021	0.787	0.046	1.76	0.065	2.49
HSP 06	0.073	0.004	5.01	0.000	0.541	0.002	2.45	0.004	5.60
HSP 07	0.079	0.004	4.87	0.002	2.06	0.002	2.68	0.005	5.93
PC HIV1 B	0.072	0.024	33.9	0.002	3.28	0.000	0.000	0.025	34.0
PC HIV2 B	3.61	0.059	1.62	0.047	1.29	0.047	1.31	0.089	2.45
PC HIV3 B	0.069	0.003	4.88	0.001	1.71	0.001	2.05	0.004	5.56
PC HIV4 B	4.11	0.071	1.73	0.047	1.14	0.064	1.56	0.107	2.59
PC HIV5 B	5.96	0.114	1.92	0.084	1.41	0.063	1.05	0.155	2.61

Overall repeatability and reproducibility for Elecsys HIV Duo (AHIVB module)

Sample	Mean	Between site	Between site	Between lot	Between lot	Reproducibility	Reproducibility
	(COI)	SD (COI)	% CV	SD (COI)	% CV	SD (COI)	% CV
HSP 01	2.70	0.000	0.000	0.056	2.07	0.080	2.96
HSP 02	22.3	0.167	0.752	0.748	3.36	0.896	4.03
HSP 03	2.60	0.007	0.267	0.189	7.25	0.197	7.57
HSP 04	22.4	0.000	0.000	0.369	1.65	0.659	2.95
HSP 05	2.62	0.000	0.000	0.053	2.01	0.084	3.20
HSP 06	0.073	0.002	2.98	0.010	13.5	0.011	14.9
HSP 07	0.079	0.004	4.61	0.010	12.9	0.012	14.9
PC HIV1 B	0.072	0.002	2.54	0.005	7.36	0.025	34.9
PC HIV2 B	3.61	0.000	0.000	0.099	2.75	0.133	3.69
PC HIV3 B	0.069	0.003	3.84	0.009	12.6	0.010	14.3
PC HIV4 B	4.11	0.000	0.000	0.218	5.30	0.243	5.90
PC HIV5 B	5.96	0.078	1.31	0.129	2.17	0.216	3.63

Analytical specificity

The effect of the following endogenous substances 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	≤ 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 HIV Duo 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 7071 fresh serum specimens and 7098 fresh plasma specimens from volunteer blood donors and 2999 plasmapheresis samples were collected at 4 donor centers. The specificities based on this study were 99.92 % (95 % confidence interval (CI) 99.81 %, 99.96 %) for the serum specimens, 99.89 % (95 % CI 99.78 %, 99.94 %) for the plasma specimens, and 100 % (95 % CI 99.87 %, 100 %) for the plasmapheresis samples.

Specificity based on assumed zero prevalence of antigen/antibody to HIV in blood and plasmapheresis donors was estimated in this study to be 99.92 % (17154/17168) with a 95 % confidence interval of 99.86 %, 99.95 %.

Specificity of Elecsys HIV Duo

Specimen category	Number tested	Number initially reactive (% of tested)	Number repeatedly reactive (% of tested)	Number positive by supplemental testing	Specificity (%) (95 % CI)
Volunteer blood donors - serum	7071	6 (0.08)	6 (0.08)	0 (0.00)	99.92 (99.81, 99.96)
Volunteer blood donors - plasma	7098	8 (0.11)	8 (0.11)	0 (0.00)	99.89 (99.78, 99.94)
Plasmapheresis donors - plasma	2999	0 (0.00)	0 (0.00)	0 (0.00)	100 (99.87, 100)
Total donors	17168	14 (0.08)	14 ^{A)} (0.08)	0 (0.00)	99.92 (99.86, 99.95)

- A) Repeatedly reactive specimens were further tested using the following supplemental assays: (HIV1) Group M RNA, HIV1 Group O RNA, Human Immunodeficiency Virus Type 2 (HIV2) RNA qualitative immunochromatographic HIV1/HIV2 antibody assay. 14 specimens were repeatedly reactive and 13 of those were confirmed negative. 1 specimen was inconclusive due to a supplemental test system flag; however, this sample was included for specificity calculation based on non-reactive results with the comparator assay and NAT. The final status was determined to be negative, for a total of 14 confirmed negative.

Clinical sensitivity

A total of 1977 HIV confirmed-reactive specimens from the categories shown in the table below were tested using the Elecsys HIV Duo assay at 3 clinical sites. Repeatedly reactive specimens were confirmed with an FDA-approved HIV-Ag-Ab assay and/or a reactive HIV NAT against the final HIV status. Sensitivity was estimated to be 100 % (1977/1977) with a 95 % confidence interval of 99.81 % to 100 %.

Sensitivity of Elecsys HIV Duo

Specimen category	Number tested	Number positive	Number repeatedly reactive (% of repeatedly reactive)	Number repeatedly reactive that were positive (% of repeatedly reactive)	Sensitivity (%) (95 % CI)
All samples known to be positive for antibodies to HIV-1	1409	1409	1409 (100)	1409 (100)	100 (99.74, 100)
All samples known to be positive for antibodies to HIV-2	200	200	200 (100)	200 (100)	100 (98.17, 100)
HIV-1 antigen positive / antibody negative	52	52	52 (100)	52 ^{A)} (100)	100 (93.15, 100)
HIV-1 viral lysates (Group M subtypes)	90	90	90 (100)	90 (100)	100 (95.98, 100)
HIV-1 Group O	50	50	50 (100)	50 (100)	100 (92.89, 100)
Individuals at high risk of HIV-1/2 infection	1410	162	168 (11.91)	162 (96.43)	100 (97.75, 100)
Individuals at low risk of HIV-1/2 infection	6910	14	21 (0.30)	14 (66.66)	100 (76.84, 100)
Total	10121	1977	1990 (19.66)	1977 (99.34)	100 (99.81, 100)

- A) One sample for this specimen category QNS for repeat testing so the respective certificate of analysis was used to provide objective evidence of HIV infection.

Analytical sensitivity

Analytical sensitivity of Elecsys HIV Duo for detection of HIV-1 p24 antigen was evaluated using the WHO International Standard HIV-1 p24 antigen, NIBSC code 90/636. HIV-1 p24 antigen was diluted with HIV negative serum and measured with Elecsys HIV Duo. Seven dilution steps of each standard were prepared and measured. Sensitivity was calculated using the mean of 3 lots tested by reading off the concentration at the cutoff from the HIV-Ag reference standard curve. The analytical antigen sensitivity of Elecsys HIV Duo as measured by WHO International Standard HIV-1 p24 antigen, NIBSC code 90/636 was shown to be ≤ 1 IU/mL. Using 3 reagent lots of Elecsys HIV Duo, results were 0.393, 0.395 and 0.389 IU/mL (average 0.392 IU/mL).

Group and subtype detection

A total of 58 viral lysates, positive for different HIV-1 subtypes, CRFs, and HIV-2 in HIV negative serum as well as HIV-1 antibody positive human serum or plasma, were tested and detected with Elecsys HIV Duo. To assess HIV-1 p24 antigen and HIV-1 antibody reactivity of HIV-1 Group N and P, a single dilution of viral lysate positive for different HIV-1 Group N and Group P in HIV negative serum as well as HIV-1 antibody positive human serum or plasma was tested and detected with Elecsys HIV Duo.

Seroconversion panels

Seroconversion sensitivity of the Elecsys HIV Duo assay was shown by testing 50 commercially available seroconversion panels comparing Elecsys HIV Duo results to the FDA-approved product. Representative results from 5 panels are summarized in the table below.

Elecsys HIV Duo assay reactivity in seroconversion panels

Panel/Donor	Days since first bleed	Elecsys HIV Duo Lot 1	Elecsys HIV Duo Lot 2	Elecsys HIV Duo Lot 3	FDA-approved product
0600-271	0	0.171	0.161	0.169	0.100
0600-271	3	0.436	0.425	0.387	0.600
0600-271	7	32.4	33.7	24.2	39.7
0600-271	10	20.0	19.9	14.7	25.2
0600-271	14	68.8	69.5	48.1	64.9
0600-271	18	11.8	11.3	8.63	13.1
0600-271	21	12.8	11.9	9.46	11.2

Elecsys HIV Duo



Panel/Donor	Days since first bleed	Elecsys HIV Duo Lot 1	Elecsys HIV Duo Lot 2	Elecsys HIV Duo Lot 3	FDA-approved product
0600-271	25	14.9	13.6	11.1	19.0
9011	0	0.188	0.175	0.170	0.090
9011	4	0.169	0.176	0.173	0.110
9011	9	0.166	0.185	0.161	0.070
9011	11	0.181	0.180	0.171	0.230
9011	16	0.171	0.183	0.174	0.160
9011	18	0.162	0.182	0.181	0.110
9011	23	0.162	0.161	0.170	0.110
9011	25	0.178	0.153	0.157	0.080
9011	30	0.386	0.380	0.387	0.210
9011	38	7.05	7.38	7.01	3.78
9011	40	10.5	11.0	10.3	5.12
9012	0	0.165	0.165	0.176	0.100
9012	2	0.171	0.190	0.178	0.070
9012	7	0.181	0.186	0.168	0.080
9012	9	0.188	0.174	0.176	0.110
9012	14	0.874	0.897	0.861	0.370
9012	16	2.99	3.11	2.95	1.02
9012	21	58.0	60.5	56.3	15.2
9012	23	138	143	135	50.0
PRB961	0	0.187	0.159	0.167	0.100
PRB961	5	0.176	0.176	0.163	0.100
PRB961	7	0.161	0.181	0.168	0.100
PRB961	12	0.165	0.188	0.176	0.100
PRB961	14	0.183	0.185	0.190	0.100
PRB961	19	0.180	0.187	0.164	0.100
PRB961	21	0.190	0.184	0.199	0.100
PRB961	27	12.4	13.0	12.5	8.80
PRB961	29	46.5	48.1	46.1	28.7
PRB966	0	0.158	0.171	0.174	0.100
PRB966	2	0.158	0.175	0.167	0.200
PRB966	20	0.166	0.163	0.172	0.200
PRB966	22	0.175	0.156	0.172	0.100
PRB966	30	0.177	0.175	0.172	0.200
PRB966	35	0.176	0.176	0.179	0.200
PRB966	37	0.227	0.246	0.248	0.300
PRB966	44	5.65	6.00	5.49	2.10
PRB966	48	2.04	2.04	1.90	2.10
PRB966	51	17.7	16.9	14.4	9.60

Other specimen conditions and disease states

100 samples containing potentially interfering factors were tested with the Elecsys HIV Duo assay comprising specimens:

- containing antibodies against HAV, HBV, HCV, HTLV-I/II, CMV, EBV, HSV-1/2, Rubella, Rotavirus, Smallpox, VZV
- containing autoantibodies (ANA) and elevated titers of rheumatoid factor
- containing antibodies against *Candida sp.*, *Escherichia coli*, *Plasmodium falciparum/vivax*, *Mycobacterium tuberculosis*, *Chlamydia trachomatis*, *Treponema pallidum* (syphilis)
- after vaccination against HAV, HBV and influenza
- from patients with monoclonal gammopathy and multiple myeloma/lymphoma, common cold, Graves' disease, Crohn's disease

- from pregnant women 1st, 2nd and 3rd trimester, multiparous pregnancies

Testing was conducted with neat specimens and aliquots individually spiked with HIV-1 antibody, HIV-2 antibody and HIV-1 p24 antigen. Results showed no interference from the above agents.

Performance characteristic of cadaveric specimen testing

Storage

Performance has been established for the use of cadaveric serum specimens (including specimens collected post-mortem, non-heart-beating) that have been collected up to 24 hours after death.²⁰ Follow general standards and/or regulations for collection, storage, and handling.

If specimens are not processed directly after initial centrifugation, it is recommended to remove the supernatant from the clot, red blood cells, or separator gel until further processing.

Cadaveric samples off-the-clot are stable for 3 days at 15-30 °C, 14 days at 2-8 °C, and 1 month at -20 °C (± 5 °C). Samples off-the-clot may be frozen up to 5 times.

Specimen category	Storage at 15-30 °C 3 days Recovery vs. t=0	Storage at 2-8 °C 14 days Recovery vs. t=0	Storage at -20 °C (± 5 °C) 1 month Recovery vs. t=0	Freeze/Thaw 5 cycles Recovery vs. t=0
Cadaveric non-reactive [mean Δ COI]	-0.0006	-0.003	0.006	0.0003
Cadaveric HIV-1 p24 Ag reactive [mean % recovery]	98.4	99.1	98.6	99.0
Cadaveric anti-HIV-1 Group M reactive [mean Δ COI]	100	101	101	97.6
Cadaveric anti-HIV-1 Group O reactive [mean Δ COI]	97.8	100	100	98.2
Cadaveric anti-HIV-2 reactive [mean Δ COI]	99.3	99.6	101	97.5

Reproducibility

20 cadaveric donor serum specimens and 20 living donor serum specimens were spiked with human plasma reactive for p24 antigen, HIV-1 group M antibody, HIV-2 antibody or HIV-1 group O antibody to create low level reactive specimens. Each specimen was tested once per day for 6 days using 3 lots of the Elecsys HIV Duo assay. Reproducibility in % CV of each specimen category was determined.

Overall reproducibility for Elecsys HIV Duo

Specimen category ^{A)}	Number tested	Mean (COI)	Reproducibility SD (COI)	Reproducibility % CV
Cadaveric donor HIV-1 p24 Ag	360	2.61	0.221	8.45
Living donor HIV-1 p24 Ag	360	2.31	0.286	12.40
Cadaveric donor anti-HIV-1 Group M	360	2.20	0.164	7.45
Living donor anti-HIV-1 Group M	360	2.20	0.124	5.63
Cadaveric donor anti-HIV-1 Group O	360	2.29	0.0905	3.96
Living donor anti-HIV-1 Group O	360	2.26	0.0764	3.38
Cadaveric donor anti-HIV-2	360	2.31	0.148	6.44
Living donor anti-HIV-2	360	2.36	0.155	6.58

A) Cadaveric serum specimens were collected up to 24 hours after death

Clinical specificity

Specificity was determined by testing 55 cadaveric serum specimens and 55 living donor serum specimens. Each specimen was tested once using 3 lots of the Elecsys HIV Duo assay.

Overall specificity of Elecsys HIV Duo

Specimen category ^{A)}	Number tested	Number non-reactive (% of tested)	Number repeatedly reactive (% of tested)	Specificity (%) (95 % CI)
Cadaveric donor - Lot 1	55	55 (100)	0 (0.00)	100 (93.47, 100)
Cadaveric donor - Lot 2	55	55 (100)	0 (0.00)	100 (93.47, 100)
Cadaveric donor - Lot 3	55	55 (100)	0 (0.00)	100 (93.47, 100)
Living donor - Lot 1	55	55 (100)	0 (0.00)	100 (93.47, 100)
Living donor - Lot 2	55	55 (100)	0 (0.00)	100 (93.47, 100)
Living donor - Lot 3	55	55 (100)	0 (0.00)	100 (93.47, 100)

A) Cadaveric serum specimens were collected up to 23 hours after death

Analytical sensitivity

Cadaveric serum specimens and living donor serum specimens were spiked with human plasma (anti-HIV-1 Group M and anti-HIV-1 Group O), serum (anti-HIV-2) and p24 cell culture supernatant, reactive for HIV Duo to create low-level reactive specimens. Each specimen was tested once, using each of 3 lots of the Elecsys HIV Duo assay. All specimens were reactive on all 3 reagent lots.

Specimen category ^{A)}	Number tested	Mean (COI)	Number positive (% of tested)	Sensitivity (%) (95 % CI)
Cadaveric donor - Lot 1 HIV-1 p24	55	3.37	55 (100)	100 (93.47, 100)
Cadaveric donor - Lot 2 HIV-1 p24	55	3.32	55 (100)	100 (93.47, 100)
Cadaveric donor - Lot 3 HIV-1 p24	55	3.62	55 (100)	100 (93.47, 100)
Living donor - Lot 1 HIV-1 p24	55	2.86	55 (100)	100 (93.47, 100)
Living donor - Lot 2 HIV-1 p24	55	2.74	55 (100)	100 (93.47, 100)
Living donor - Lot 3 HIV-1 p24	55	2.93	55 (100)	100 (93.47, 100)
Cadaveric donor- Lot 1 anti-HIV-1 Group M	55	2.98	55 (100)	100 (93.47, 100)
Cadaveric donor- Lot 2 anti-HIV-1 Group M	55	3.09	55 (100)	100 (93.47, 100)
Cadaveric donor- Lot 3 anti-HIV-1 Group M	55	3.14	55 (100)	100 (93.47, 100)
Living donor - Lot 1 anti-HIV-1 Group M	55	3.20	55 (100)	100 (93.47, 100)
Living donor - Lot 2 anti-HIV-1 Group M	55	3.19	55 (100)	100 (93.47, 100)
Living donor - Lot 3 anti-HIV-1 Group M	55	3.22	55 (100)	100 (93.47, 100)
Cadaveric donor - Lot 1 anti-HIV-1 Group O	55	2.44	55 (100)	100 (93.47, 100)
Cadaveric donor - Lot 2 anti-HIV-1 Group O	55	2.47	55 (100)	100 (93.47, 100)
Cadaveric donor - Lot 3 anti-HIV-1 Group O	55	2.54	55 (100)	100 (93.47, 100)

Specimen category ^{A)}	Number tested	Mean (COI)	Number positive (% of tested)	Sensitivity (%) (95 % CI)
Living donor - Lot 1 anti-HIV-1 Group O	55	2.66	55 (100)	100 (93.47, 100)
Living donor - Lot 2 anti-HIV-1 Group O	55	2.51	55 (100)	100 (93.47, 100)
Living donor - Lot 3 anti-HIV-1 Group O	55	2.66	55 (100)	100 (93.47, 100)
Cadaveric donor - Lot 1 anti-HIV-2	55	3.48	55 (100)	100 (93.47, 100)
Cadaveric donor - Lot 2 anti-HIV-2	55	3.30	55 (100)	100 (93.47, 100)
Cadaveric donor - Lot 3 anti-HIV-2	55	3.17	55 (100)	100 (93.47, 100)
Living donor - Lot 1 anti-HIV-2	55	3.70	55 (100)	100 (93.47, 100)
Living donor - Lot 2 anti-HIV-2	55	3.32	55 (100)	100 (93.47, 100)
Living donor - Lot 3 anti-HIV-2	55	3.28	55 (100)	100 (93.47, 100)

A) Cadaveric serum specimens were collected up to 24 hours after death

Additional information

For further information, refer to the User Guide for the corresponding analytical unit and to the Method Sheets of all necessary components (if available in your country).

Report any serious incident that has occurred in relation to the device to the manufacturer and the competent authority of the member state in which the user and/or patient is established.


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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.

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Change log

Due to technical reasons, changes that have been made since the last version of this document are listed in the following table instead of indicated by change bars in the margin.

Document Revision Information

Doc. Rev. 4.0	Cadaveric claims were added to the following new and existing sections: Intended use, Specimen collection and preparation, Limitations of the test, Performance characteristics of cadaveric specimen testing, and References Editorial and layout updates due to change in software.
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